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SLEEP WAKEFULNESS DETERMINATIONS FROM HEART RATE DATA. VOLUME I--ETC(U)

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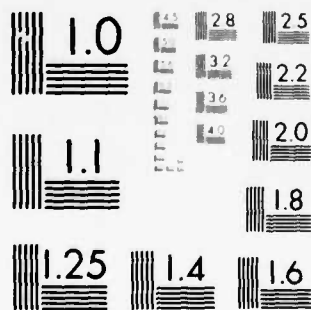
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**SLEEP-WAKEFULNESS DETERMINATIONS
FROM HEART RATE DATA**

by

A012275

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May 31, 1977

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ABSTRACT

During the past years several projects have been conducted at the University of Texas at Austin by members of the Bio-Medical Engineering Program investigating the automated classification of levels of wakefulness. The primary design and goal of these projects was rapid, inexpensive determination of levels of wakefulness performed accurately using easily derived physiologic parameters. It was felt that by combining some of the procedures and results of previous studies with the procedures developed from the last two years of this research, a conglomerate algorithm which had the capabilities desired could be developed.

During the third year of this research, an altered algorithm has been developed from previous algorithms to classify REM⁺ - NREM sleep stages from minute-by-minute heart rate. One night of data was used from each of two subjects as training data for our algorithm. The other nights of these two subjects and all the data from a third subject were used as test data. Subjects LES and FER were used as training and test subjects, while subject OWN supplied only test data.

The reclassification of the two training nights yielded accuracies of 51.30% and 63.68% for night one of LES and night one of FER, respectively. Accuracies from the remaining data of subject LES yielded 60.11% to 66.50%, of subject FER 45.99% to 63.68%. Subject OWN, whose data were not used in any training, yielded accuracies from 52.27% to 58.60%.

We concluded from our study that the method of analysis we developed and the results we obtained were sufficient to warrant further investigation. We did achieve one of our primary goals: the reduction of cost, volume, and complexity in automated classification of levels of wakefulness. We feel that further development of an automated process algorithm for the accurate determination of levels of wakefulness can be fulfilled in the foreseeable future.

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CHAPTER I

INTRODUCTION

Sleep is commonly looked upon as a periodic temporary cessation, or interruption, of the waking state, which is the prevalent mode of existence for the healthy human adult.⁴⁹ While a satisfactory short definition of sleep is lacking, Pieron⁴⁹ considered it a suspension of sensory-motor activities characterized by an almost complete absence of movement and an increase in the thresholds of general sensitivity and of reflex irritability. Pieron added two qualifications to the above definition. The first is that the suspension of activity be dependent upon internal necessity and not on external conditions. The second qualification is the preservation of the ability to be aroused or awakened, thus differentiating it from states such as coma, trance, and anesthesia.

The study of the phenomena of sleep has occupied researchers for many years. Since the advent of the polygraph and the advancement of the digital computer, many researchers have expanded efforts toward the development of new automated methods for the quantitative analysis of sleep patterns. Almost exclusively, these efforts have been directed toward computer aided detection of characteristic changes in EEG sleep patterns.^{54,67,27,56}

Typically, the methods used to examine the EEG sleep patterns involve the analysis of definitive measures such as frequency and amplitude components of the EEG. These EEG measures are then applied to automated procedures for classification of sleep patterns using either analog, digital, or hybrid computers.

In the last few years, our research team at the Bio-Medical Engineering Heart Rate Laboratory has conducted a number of research projects dedicated toward development of automated methods for the clas-

sification of sleep patterns.^{1,76,77,52,56} Our primary goal has been the development of a sleep pattern detection process using an easily derived physiologic parameter coupled with a rapid, inexpensive algorithm for quantitative analyses. Instead of the typically used EEG, we have chosen beat-by-beat heart rate as our physiologic parameter. Several researchers have reported that heart rate does exhibit concomitant characteristic changes with changes in sleep depth.^{1,14,20,68} We chose beat-by-beat heart rate as our criteria because the ECG is an easily derived physiologic parameter which is more in keeping with our desire for low-cost and limited data bulk.

CHAPTER II

BACKGROUND

Characteristic Patterns of Sleep

Sleep has been described as a "diminished...sensitivity to external stimuli";³⁹ a "state of vulnerability";²⁴ an innate, automatic, exigent, and essential process;³⁹ an active process,^{24,39} and a state of "restoration and recovery".²⁴ It is said to be internally regulated and under strict central nervous control.³⁹

Whatever the function or definition, it is well known that certain physiological phenomena are associated with the sleeping state.

Objective observation of sleep phenomena really came to light with the advent of the electroencephalograph. By placing electrodes on various positions of the skull, it was found that electrical activity of the brain could be recorded. Electroencephalographic (EEG) patterns exhibited definitive characteristics in both the waking and the sleeping states.

Descriptions of such patterns have employed objective terms such as "alpha", "beta", "delta", and "theta waves"; "low voltage fast sleep"; "high voltage slow sleep"; "spindle activity"; and "K-complexes".

With the discovery of ocular motility during sleep,^{5,6,26,65} another device was employed for objective observation. The electrooculograph (EOG), measures electrical activity caused by eye movements. When it was discovered that there was a high degree of correlation between certain EEG and EOG patterns, the phenomena of REM (rapid eye movement) sleep was described.⁶

From these findings researchers have developed standard procedures for "scoring" EEG patterns into different depths during sleep, where depth is associated with lack of response to external stimuli. The classical technique for determining sleep levels or stages involves the clinical interpretation of the concomitant changes in EEG and EOG patterns on a

continuous basis. This requires the tedious, expensive and time-consuming task of scoring literally miles of charts.

Nevertheless, these methods have provided us with quantitative techniques of research and have allowed us to perform scrupulous analyses of sleep and its related phenomena.

Sleep is typically divided into four primary stages of depth: Stages 1, 2, 3, and 4 with Stage 4 representing the deepest sleep.²³ It was found that REM sleep produced the same EEG patterns as Stage 1 and thus Stage 5 is sometimes used to denote combined Stage 1 and REM sleep. Awake is labeled Stage 0. Characteristic EEG and EOG patterns of these stages are shown in Fig. 1.⁴⁸ A graphical representation of staging throughout an entire night of sleep is shown in Fig. 2.⁵³ This figure shows the subject progressing from awake to Stage 4 and then returning to Stage 1, 5 which is Stages 1 and 5 combined. This is typical of a night of sleep. The horizontal bars above Stage 1, 5 indicate the simultaneous occurrences of rapid eye movements or Stage 5. It can also be seen that the subject makes a similar progression from light to deep sleep throughout the night. This "cycling" occurs approximately every 60-100 minutes and has been described in numerous other reports.^{1, 15, 16, 23, 48, 62, 80} We have defined the cycles as beginning at the onset of a REM period (horizontal bars) and ending at the onset of the next REM period, except for Cycle 0 which typically begins with Stage 1 without concurrent eye movements. This subject produced five complete cycles during this night of sleep.

Another phenomena of cycling is that the "trough" of the cycle gets more shallow as the night progresses which is also typical of a normal night of sleep.^{23, 48} In general, progression from "wakefulness to Stage 4 at the beginning of Cycle 0 is a continuum of change while reversion to the lighter stages at the end of a cycle are quite abrupt.²³ Stages 3 and 4 are only occasionally reached during cycles following the second.²³

SLEEP EEG PATTERNS

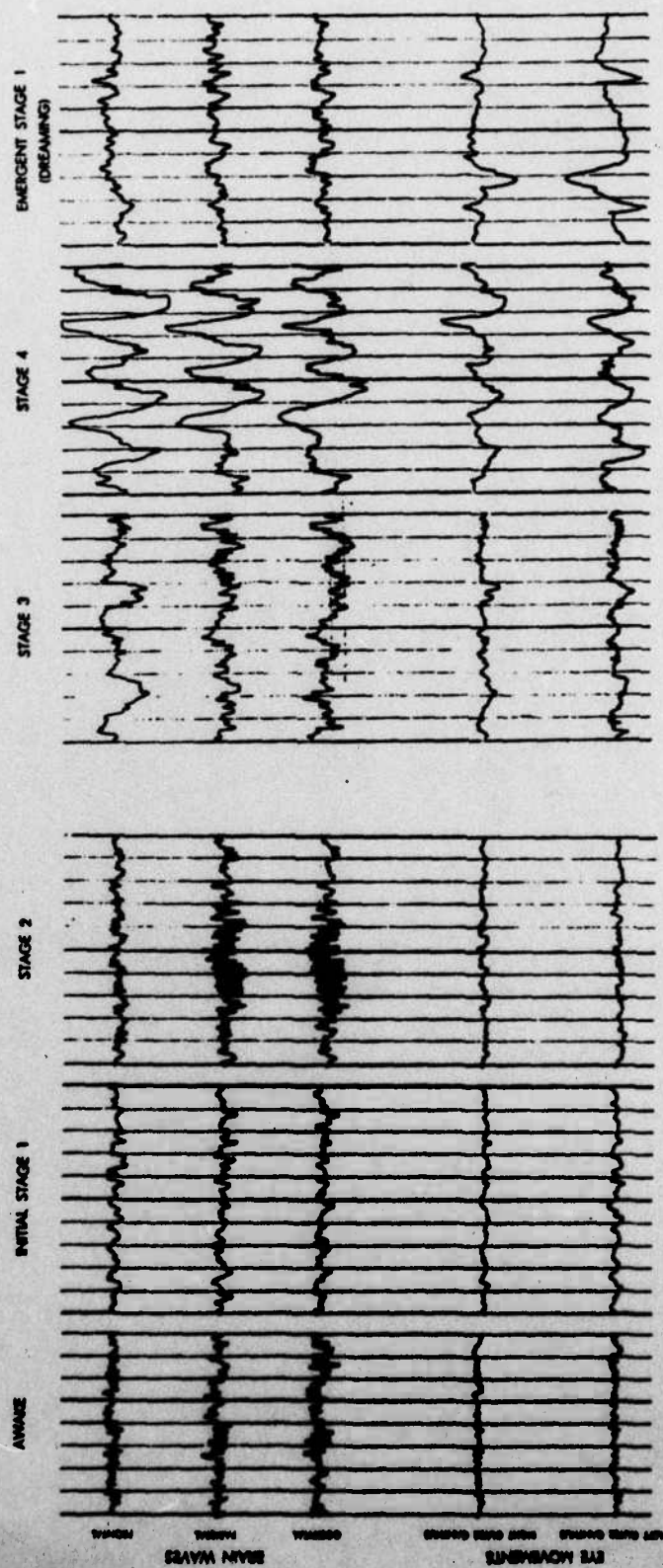


Figure 1.

A TYPICAL NIGHT OF SLEEP

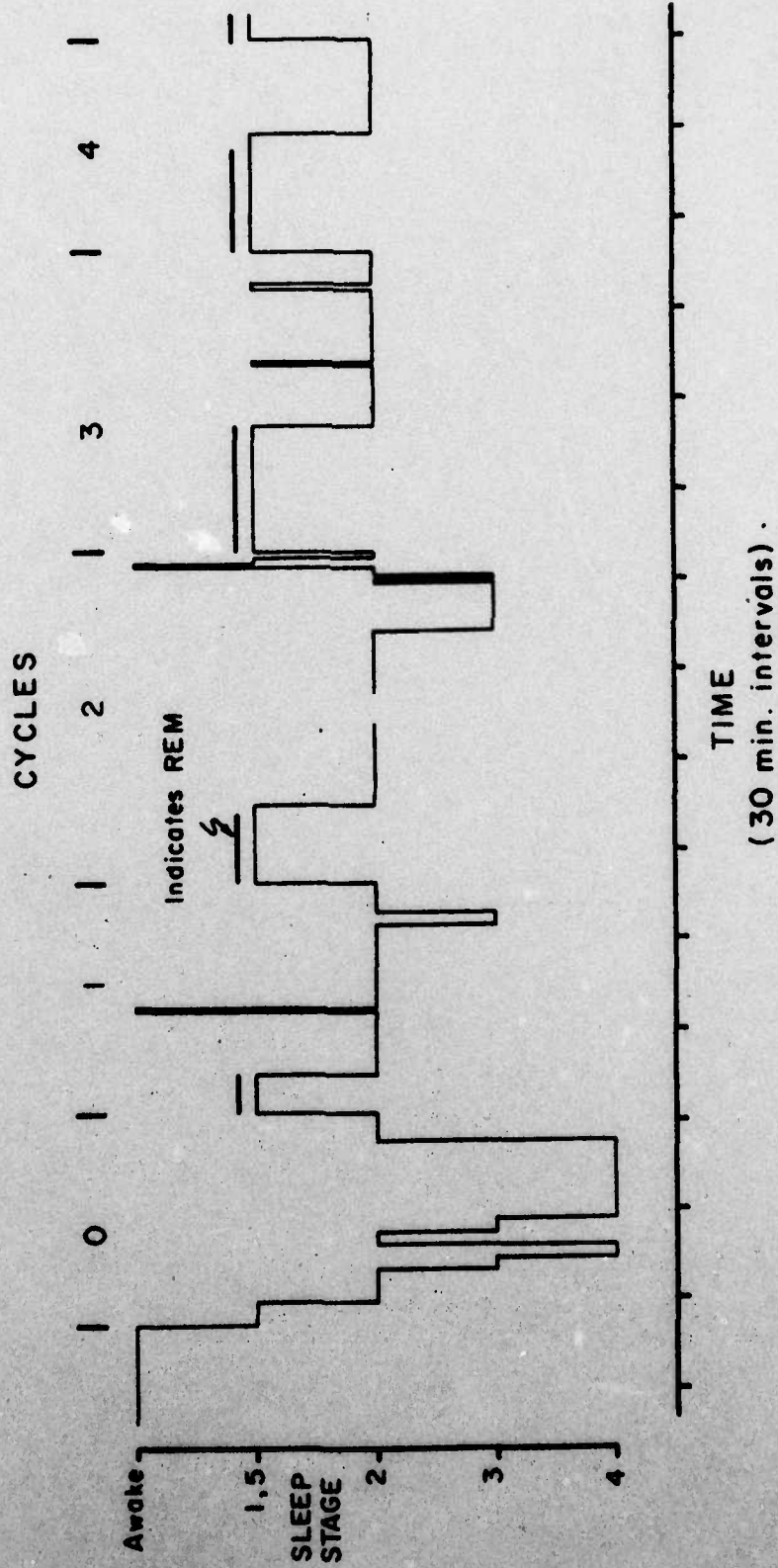


Figure 2.

Another characteristic is that sleep patterns differ in other respects when considering sleep near the beginning of the night as opposed to that near waking time.⁵ For example, the length of the REM periods tends to increase toward the end of the night while NREM (Non-REM) durations decrease.^{19,37} Agnew and Webb³ also reported the increased length of REM periods towards the end of the night. They reported several other findings concerning the time course of events with reference to REM sleep. Age appeared to be a primary determinant of the REM amount of sleep up to the early teens, but has little effect thereafter. The length of prior wakefulness appeared to have little or no effect on the amount of REM sleep. They also found that the longer the sleep time, the greater the amount of REM sleep. The findings of Agnew and Webb³ agreed with those of Moses et al.⁵⁹ in that REM sleep occurred mainly in the last half of the night and the number and length of REM episodes increased in the last half of the night. Both studies also found that the interval between REM episodes decreased in the last half of the night.

It is known that sleep patterns in man differ from those in other mammals in some aspects;⁷⁴ however, sleep in man is relatively consistent in nature from one subject to the next. Age also plays another important role in characteristics of sleep.²⁹

It should be remembered that although sleep is described in quantitative measures of "stages", sleep patterns are associated with continuous processes and do not always lend themselves to discrete classification. In other words, there are fluctuations of depth within each stage as well.^{23,86}

Heart Rate and Other Autonomic Activity Associated with Sleep

Other physiological variables are known to be associated with changes in sleep patterns, especially heart rate. In fact, depth of sleep is said to take on different meanings according to the variables used to define it^{23,86} and the determination of depth should take into account

the simultaneous fluctuations in heart rate, blood pressure, respiration, and even skin potential response.^{8,9,18,23} Variables such as gastric motility, metabolic rate, penile erections, peripheral muscle activity and pupillary reactions have also been regarded as autonomic correlates in sleep.^{4,24,49,74,86} Before the advent of the polygraph, autonomic variables were the only means for describing sleep.⁸⁶

Although there has been much disagreement among researchers regarding the significance of the autonomic correlates, most tend to agree that the following observations consistently hold true.

1. In general, the trend is for heart rate, blood pressure, and respiratory rate to decrease with increasing depth of sleep.
2. The most readily observable phenomena of these three activities is the change in variability with change in depth.
3. Of all the autonomic correlates, changes in heart rate are probably the most consistent measures of sleep depth.
4. Gross body movements also exhibit cyclic variations closely associated with the sleep cycles.
5. Skin potentials generally increase with the onset of deep sleep and are markedly reduced during REM sleep.
6. All of these correlates follow complex patterns which are under control of the autonomic nervous system.

The slowing of the heart is a consistent phenomena associated with the onset of sleep and has been found to reduce in rate from 2 to 12 beats per minute on the average depending on other factors such as sex and age.⁴⁹ However, the minimum heart rate in the normal waking state was found to be less than the maximum rate in sleep indicating that overlapping of the heart rates are common.⁴⁹ On the average, the range of heart rate is lower during sleep than during waking.⁴⁹ Virtually all researchers agree that the variability of heart rate is the most pronounced feature when

considering different depths of sleep.^{1,4,13,16,73,75,86} Fluctuations in heart rate are pronounced during the light stages, Stage 1, 2 and REM, and yet also contains periods of complete quiescence in variability.^{13,73} Brooks et al.¹⁶ reported that cardiac acceleration from any sleep stage to a lighter stage appeared to be proportional to the change in depth. For example, they observed a 10% increase when changing depth by one stage, e.g., Stage 4 to 3 or Stage 3 to 2, and a 13.7% increase when changing two stages, e.g., Stage 4 to 1 or Stage 3 to awake. Using low-birthweight infants as subjects, Watanabe et al.⁷⁹ also found significant differences ($p < .01$) in the range of variation when comparing Stage 1 with 2 or 3, Stage 2 with 3, and Stage 2 with REM. The ranges during the deeper stages were significantly lower. Snyder et al.⁷³ reported an average of 55% increase in their variability index during REM over Stage 2. Aldredge's et al.¹ study tended to confirm these results. They found that, in general, the standard deviation of heart rate for REM was significantly higher than for Stage 2 which was in turn significantly higher for Stages 3/4 combined within a given sleep cycle. These relationships did not necessarily hold true when comparing cycles.

Average heart rate shows significant change with change in sleep patterns, but is not as pronounced as the variability measures. Snyder et al.⁷³ when not controlling for time of night, found a significant decrease ($p < .001$) in heart rate from REM to Stage 2 with an average change of about 4 beats/minute. They also reported Stages 3/4 heart rate to be significantly higher ($p < .001$) than Stage 2. When controlling for time of night where the difference between Stage 2 and Stages 3/4 was no longer significant, Khatri et al.⁴⁷ found average heart rate to decrease from the awake control an average of 4.6 beats/min for Stage 2 (significant at $p < .02$) and 5.1 beats/min for Stages 3/4 (significant at $p < .01$). They also found a significant increase ($p < .01$) in heart rate when entering REM sleep. Aldredge et al.¹, on the other hand, found that changes to lighter stages produced significant increase in

average heart rate within a cycle, but this relationship did not always hold when comparing, say REM of one cycle with Stage 2 of another cycle.

On the other hand, some researchers implied that heart rate changes on the average were insignificant.^{4,75}

Blood pressure and respiratory rate follow similar patterns and trends as heart rate.⁹ The consensus is that blood pressure and respiration show high degrees of variability during REM sleep and become more stable in the deeper stages. On the average, blood pressure and respiratory rate during REM are significantly higher.^{4,20,37,47,73,86} Blood pressure tends to reach a minimum during the first third of sleep and is probably associated with Stages 3 and 4 which occur almost exclusively during this period.^{49,73} Respiratory changes, such as increased rate and decreased amplitude have been correlated with REM bursts (periods when eyes are actually moving).^{4,7}

Body movements cycle from relatively few during deep sleep to a marked increase in number just before REM. The REM period is characterized by no peripheral activity, but movement begins again immediately after REM and then returns to quiescence with deepening sleep.^{23,25}

Changes in skin responses during sleep, known as the Tarchanoff effect, is characterized by increased response with deep sleep and a marked decrease in response due to increased threshold in REM sleep.^{18,86}

Changes in autonomic activities such as heart rate, blood pressure, and respiratory rate are thought to follow complex patterns mediated through parasympathetic and sympathetic neural control.^{8,47} In some cases, these variables appear to be interdependent upon one another. For example, Bond et al.¹³ found that heart rate variability during Stages 1 and 2 was rhythmic and roughly associated with respiration. During deep sleep there appeared to be a precise correlation between heart rate variability and respiratory frequency. However, during REM there was total dissociation with irregular variability. Snyder et al.⁷³ also reported

that heart rate, blood pressure, and respiration "oscillated quite regularly around a relatively stable base line" during Stages 2 and 3/4 combined, while Stages 1/REM combined featured wide and erratic fluctuations. They reported many instances where changes in all three variables occurred together and other instances of independent changes. They suggested that simultaneous changes in these variables may be secondary responses to changes in respiration. Baust et al.⁸ performed very thorough experiments on parasympathetic and sympathetic influences on heart rate during sleep in the cat. They concluded that the phasic changes in heart rate during desynchronized (REM) sleep and wakefulness are decisively induced by vagal influences. In general, they found that the fall in heart rate from wakefulness to synchronized sleep was mainly due to increased parasympathetic activity and that phasic changes during REM bursts were associated with phasic events in both parasympathetic and sympathetic activity. In other words, both types of autonomic activity play roles in physiologic changes during sleep.

Control of these autonomic variables have been theorized to lie with parasympathetic and sympathetic activity, dream-arousal activity, biochemical mechanisms, and a central nervous system "triggering" mechanism. Whatever the mechanism, these variables consistently undergo functional changes during the sleeping state.

Automated Detection of Sleep Stages

Larsen et al.⁵¹ probably best describes the reasons behind the search for automated methods of detecting sleep stages. Now that there is some general agreement as to what quantitative measures describe the different stages of sleep, Larsen felt that other than eliminating the tedious task of visual scoring, automated methods have a two-fold theoretical value:

- (1) to provide a better understanding of the physiological aspects of sleep,
- (2) and to test the adequacy of variables thought to contain quantitative information about sleep.

Predominantly these methods involve seeking out the definitive measures of the EEG (e.g., frequency components) and then developing some analog, digital, or hybrid method to use these measures for classification. In essence, researchers have attempted to devise automated models of pattern recognition especially designed for sleep patterns of the EEG.

Approaches to the solution of the problem have employed techniques in spectral analysis,^{36,50,57,64} period analysis,⁷⁰ and baseline cross analysis.^{40,51,83} These procedures have met with only limited success, except for a hybrid system developed by Gaillard et al.³⁰ who reported overall accuracies (when compared to visual scoring) up to 92.31%. An overview of the results of several studies is shown in Table 1. Problems in classification are cited as overlap of measures of discrimination,⁷⁰ the need for inclusion of more measures,^{40,57,70} imprecise definition of variables,⁴⁰ unreliability of visual scoring,⁵⁷ and the need for additional methods of analysis.⁵⁷

Although all of these methods were considerably faster in detection than visual scoring, they still did not resolve the problem of input bulk. For example, sampling rates ranged from 100 to 500 samples per second. If only one channel of EEG was digitized for digital computer analysis, the data base would be enormous for a continuous 7-1/2 to 8-hour recording. This problem was somewhat resolved by analyzing only certain short portions of the entire record, but the data base was still large and possibly some information was lost. Also, the studies usually monitored ECG and EOG's as well as several EEG channels.

In summary, "...the high cost of digital computer analysis of

all-night sleep EEG's and the relatively large volume of information it produces have decreased its value. No such system of analysis has yet proved sufficiently reliable or simple to justify its frequent or routine use in all-night sleep monitoring."⁴¹

Recently, however, researchers in our program have been investigating the use of beat-by-beat heart rate as the criteria parameter. As discussed earlier, it is agreed among sleep researchers that heart rate does contain sleep information, although its use as a detection parameter has never been considered. We felt, however, that changes in beat-by-beat heart rate, as opposed to averages over long periods, can be used for detection of sleep stages if used in an optimal manner. Using heart rate certainly has advantages over previously cited measures. For example,^{53,81}

- (1) the ECG is an easily derived physiologic parameter;
- (2) practically speaking, the ECG alleviates the need of uncomfortable multiple electrodes used in monitoring the EEG which are cumbersome and restrictive of movement; and
- (3) the sampling rate is now reduced to 50-100 samples per minute which greatly reduces data input and transmission volume.

Hence, based upon what is known about heart rate and sleep, and our desire for a low-cost, easily derived input parameter of limited bulk, we have attempted to design an automated method for the classification of sleep patterns using beat-by-beat heart rate.

Table 1.

REPORTED RESULTS
OF AUTOMATED CLASSIFICATION

Stage	Roessler ⁷⁰	Lubin ⁵⁷	Larsen ⁵¹	Ittl ⁴⁰	Martin, et al. ⁵⁸
W	87%	64%	91%	74%	2.6%
1	45%	70%	64%	73%	100.0%
REM*	-	56%	66%	-	89.3%
2	63%	82%	85%	55%	89.1%
3	79%	0%	85%	62%	57.4%
4	84%	91%	85%	59%	87.8%
OVERALL	69%	60%	79%	65%	79.6%

* Most studies did not attempt to classify REM separately.

CHAPTER III

THE PROBLEM

Objective

The objective of this research still conforms to that sought in all our past studies. Stated precisely, it is the development of a process by which rapid, inexpensive determinations of levels of sleep can be performed accurately using an easily derived physiologic parameter, such as beat-by-beat heart rate.

Our Previous Work

The experimental protocol for this project is comprised of combinations of the ideas, methods, and results from our previous projects.

The first study reported, "Computer Sleep Stage Classification Using Heart Rate Data" by Welch and Richardson,⁸² was an overview of a two year research effort on the "Bandwidth Reduction of Sleep Information".^{84,85}

The choice of beat-by-beat heart rate as a parameter for sleep analysis is supported by Brook et al.,¹⁶ who stated that sleep depth is probably reflected more in changes in cardiac cycle length than in the average heart rate values. Since previous researchers felt that average heart rate, as a single measure, did not contain sufficient information for classifying sleep depth, we approached the problem with the idea of employing a multivariate technique. We devised eleven heart rate measures which included the mean and standard deviation of heart rate over set epochs and a nine interval histogram over each epoch. These descriptors were submitted to a multi-discriminant model²¹ coupled with a Bayes classifier to classify each epoch into a particular stage. This approach necessitated both a training set of data and a test set of data. The model's accuracy was decided based upon comparison with visual scoring of the EEG. The results of our efforts are

shown in Table 2. Training night accuracies ranged from 53% to 77%, while testing night accuracies ranged from 21% to 73%. These results represented only moderate success. We found that while the mean and standard deviation of heart rate were the most significant of the 11 measures, there was also a significant difference in the mean heart rate between nights one and two for several subjects.

The second report investigated "Variations of Heart Rate During Sleep as a Function of the Sleep Cycle" by Aldredge et al.¹ The basis for this study centered around the idea that "irregularities in heart rate and nightly trends have prevented any useful correlation with sleep stage"¹ and that pooled heart rate data over an entire night does not accurately represent the behavior of the individual's sleep patterns.

Sleep cycles are classically defined by Kleitman⁴⁸ as beginning at the end of a REM period and ending at the end of the next REM period. The exception is the first period which has no REM at its beginning. Preliminary results suggested we should redefine the cycle as beginning at the onset of a REM period and ending at the onset of the next REM period, since it appeared that the preceding REM period had an effect on the trends in heart rate of the succeeding stages.

Using the same data as that used in our first study,⁸² we initially divided the nights of sleep into sleep cycles based upon visual examination of the EEG patterns. Several hypotheses were examined. The first determined if the average heart rate during REM was equal for all cycles. The hypothesis of equality was applied to the standard deviation (variability) of heart rate. Other hypotheses were designed to determine if the average and variability of heart rate were equal for the different stages with any given cycle.

We found that on the average, heart rate differed from cycle to cycle while variability, as measured by the sample standard deviation, appeared to be consistent throughout the night.

Table 2.

CLASSIFICATION RESULTS REPORTED BY WELCH⁸²

<u>SUBJECT</u>	<u>NIGHT 1</u> [*]	<u>NIGHT 2</u> ^{**}
CHI	77%	73%
FAR	61%	64%
GIL	63%	54%
MOS	64%	45%
NOR	60%	37%
PAD	53%	21%
SAF	70%	40%
SCH	65%	40%

Stages 1 and REM were combined as were Stages 3 and 4.

* Training night of data

** Testing night of data

A third study which provided information for this research was that of Weber et al,⁸¹ entitled "Detection of REM 1 Sleep Stage and Eye Movement from Beat-to-Beat Heart Rate". We hypothesized that the sudden cyclic changes in heart rate seen during sleep were caused by the same neural process which caused rapid eye movements. The typical approach to the study of transient phenomena of periodic signals is spectral analysis via the Fourier transform.^{10,11,14,35}

Two data segments were constructed from one subject. One data set was made up of heart rate data, R-to-R intervals, from REM segments with concurrent conjugated eye movements and was designated REM-REM. For control, the second data set was a series of intervals from REM sleep segments during which no concurrent conjugated eye movements were observed. These data were designated REM-NREM.

A typical spectrogram was constructed from REM-REM data by autocorrelating these data segments with themselves and then Fourier transforming the autocorrelated data. Sequential epochs of the second night were similarly transformed and their spectrograms compared to the typical spectrogram. If the measure of similarity was high enough (determined empirically), then the epoch of the second night was classified as REM-REM sleep. REM-NREM segments underwent the same processes. Many variations and methods of improvement were tried with the overall best results being that Stage 1, REM was successfully detected via this method with approximately 80% accuracy for the one subject studied. We considered the technique as "tentatively successful" in detection of Stage 1, REM.

The fourth study in this series is the 1975 Annual Report "Sleep-Wakefulness Determinations From Heart Rate Data" by Lisenby et al.⁵⁴ In this study, we hypothesized a REM-NREM classification algorithm based upon the Fourier transform of heart rate data epochs. Beat-by-beat heart rate was determined by measuring the time in milliseconds between successive R-waves on the electrocardiogram. The R-to-R intervals were used

to define a function where the independent variable was heart beat number and the dependent variable was the magnitude or duration of the corresponding R-to-R interval (see Figure 3). These values were assumed to represent equally spaced samples of a continuous function. These data were divided into one minute epochs. Each epoch was represented by an array which contained the values of the Heart Beat domain and was zero filled to 128 points to facilitate use of our discrete Fourier transform routine.

Each one minute epoch of Heart Rate domain data was autocorrelated to form an autocorrelation function for each minute epoch (see Figure 4). Two stages were being examined, REM, 1 (stages Awake, 1 and 5 combined) and NREM (stages 2, 3, and 4 combined). The autocorrelation function for each minute was then Fourier transformed into the Beatquency domain (see Figure 5). The resulting spectrograms were combined and averaged to form a typical REM, 1 and a typical NREM template. Each template was normalized to a maximum amplitude of one.

The data used for the previous studies were also employed here. The first night of sleep of each of the nine subjects were used to compute Beatquency domain templates for REM and NREM categories for each subject in the manner described above. These templates were then used to reclassify their respective training nights of data as well as classifying a testing night of data (night two for each subject.) The results of this algorithm are shown in Table 3.

In a second phase of this same study⁵⁴, a multiple regression analysis model was designed to detect the individual levels of sleep: Stage 0, Stages 1/5, Stage 2, and Stages 3/4. To train this algorithm, the first step was to create a new data set containing the measures to be used as predictors. For each minute of data, eleven frequency distribution measures were formulated: the mean R-to-R interval length, the standard deviation about the mean, and a nine-interval standard Z-score histogram. These measures are listed in Table 4. Once these measures were obtained

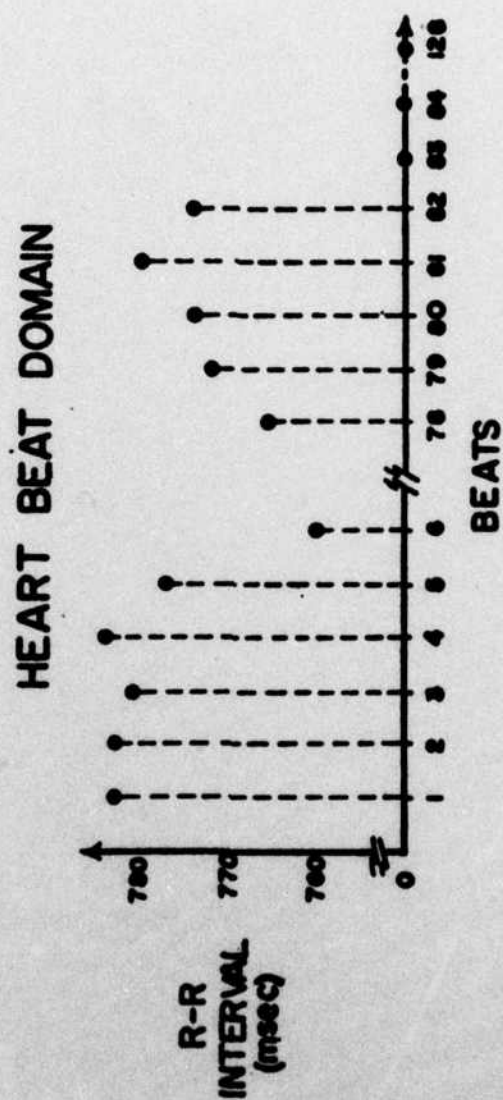


Figure 3.

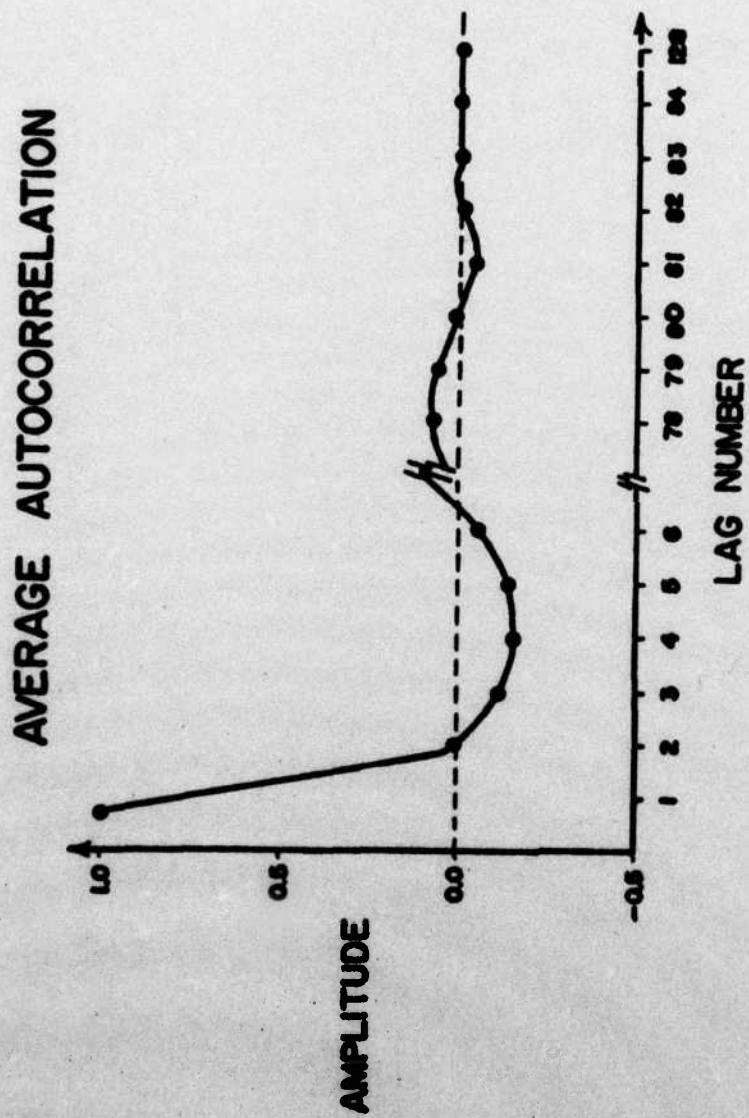


Figure 4.

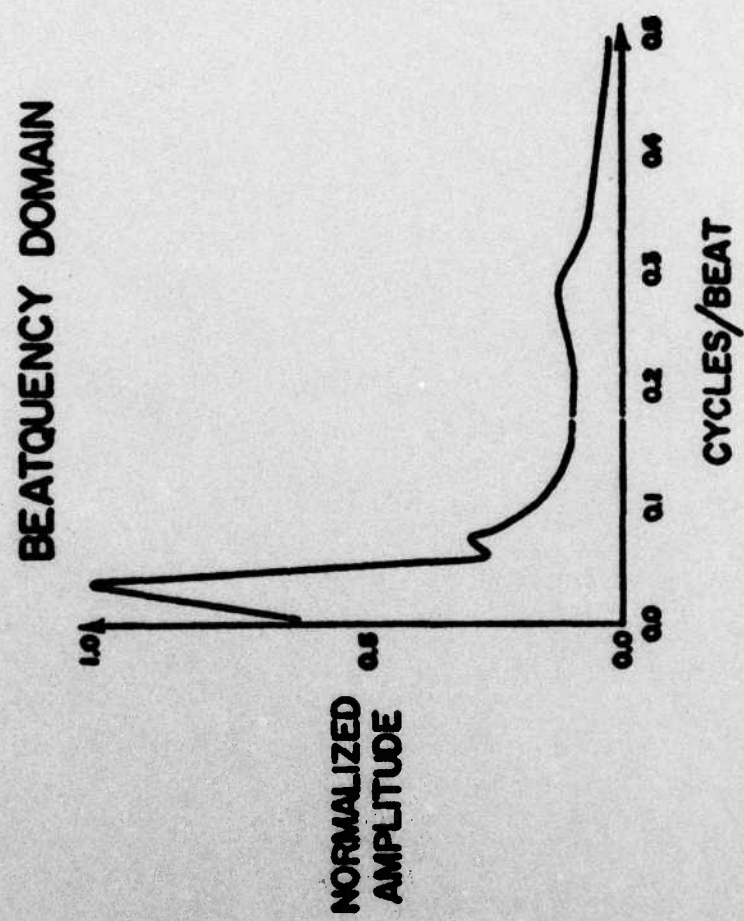


Figure 5.

Table 3.

RESULTS OF REM-NREM CLASSIFICATION⁵⁴

<u>SUBJECT</u>	<u>ACCURACY</u>
SAF 1	77.9%
SAF 2	83.9%
SCH 1	69.6%
SCH 2	81.8%
FAR 1	64.9%
FAR 2	73.9%
CHI 1	77.5%
CHI 2	73.2%
MOS 1	74.1%
MOS 2	59.6%
GIL 1	71.8%
GIL 2	55.6%
NOR 1	67.5%
NOR 2	58.9%
PHI 1	70.5%
PHI 2	63.4%
PAD 1	70.0%
PAD 2	68.6%

Table 4
REGRESSION MODEL
HEART RATE MEASURES

MEASURE NUMBER	MEASURE DESCRIPTION*
1	Mean (μ_{x_1})
2	Standard Deviation (σ_{x_1})
3	freq { $Z_{1j} < -1.75$ }
4	freq { $-1.75 \leq Z_{1j} < -1.25$ }
5	freq { $-1.25 \leq Z_{1j} < -0.75$ }
6	freq { $-0.75 \leq Z_{1j} < -0.25$ }
7	freq { $-0.25 \leq Z_{1j} < 0.25$ }
8	freq { $0.25 \leq Z_{1j} < 0.75$ }
9	freq { $0.75 \leq Z_{1j} < 1.25$ }
10	freq { $1.25 \leq Z_{1j} < 1.75$ }
11	freq { $Z_{1j} \geq 1.75$ }

*"freq { }" means the number of Z_{1j} 's that occur within the given range.

for each minute of data for each subject and each night, the Night 1 measures were applied to multiple regression analysis to obtain a series of linear regression weights. The remainder of the training procedure included re-classifying Night 1, cycle by cycle, into its respective sleep stages to determine the algorithm's accuracy.

The testing procedure for the regression models involved the formulation of the predictor measures from the Night 2 data for each subject. The regression models derived from Night 1 data were used to classify corresponding sleep cycles in Night 2. For example, the model from Night 1 for cycle 0 was used to classify sleep stages for Night 2 cycle 0. The same procedure occurred for all subsequent cycles. The results of these classifications are shown in Tables 5 and 6.

The fifth report in this study was the 1976 Annual Report, "Sleep-Wakefulness Determinations From Heart Rate Data" by Lisenby et al.⁵⁶

This report is a continuation of the work done during 1975. The data base, however, was expanded considerably by the addition of 16 nights of data from 3 subjects. This new data was supplied by the U.S. Naval Sleep Laboratory in San Diego, California. The primary work done during this year's portion of our contract involved the formulation of REM + (Stages Awake, 1, and REM combined) and NREM (Stages 2, 3, and 4 combined) spectral templates from each night of data for each of the three new subjects. These templates were then used to reclassify their respective nights of data for their respective subject. The results are shown in Tables 7 - 9. Several attempts were made at a four stage classification; however, we found difficulty separating stage Awake from a combination of Stages 1 and REM (5). This same difficulty was encountered in separating Stage 2 from a combination of Stages 3 and 4.

Table 5.

**RESULTS OF REGRESSION ANALYSIS
FOR INDIVIDUAL CYCLES**

SUBJECT LABEL	CYCLE NUMBER					
	0	1	2	3	4	5
SAF1	77.9%	89.6%	75.2%	89.0%	85.7%	77.8%*
SAF2	47.0%	60.9%	49.5%	-	-	-
SCH1	69.1%	68.5%	83.3%	76.8%	74.5%	53.8%*
SCH2	30.1%	16.5%	45.2%	70.2%	50.0%	-
FAR1	71.2%	75.5%	84.3%	85.3%	64.2%	-
FAR2	25.8%	56.6%	70.5%	71.1%	84.8%	-
CHI1	78.5%	58.6%	92.3%	90.0%	88.6%	87.2%
CHI2	70.0%	37.9%	40.9%	92.9%	80.8%	53.2%
MOS1	45.0%	84.2%	62.1%	78.2%	71.2%	-
MOS2	45.9%	51.1%	68.7%	58.8%	44.3%	77.4%**
GIL1	52.5%	71.3%	97.3%	90.3%	65.3%	71.4%*
GIL2	33.8%	56.2%	84.6%	55.4%	75.0%	-
NOR1	42.7%	87.2%	55.6%	80.6%	-	-
NOR2	44.6%	19.5%	27.0%	57.6%	57.3%**	14.6%
PHI1	58.3%	65.6%	74.0%	62.0%	-	-
PHI2	27.3%	62.5%	56.3%	23.5%	-	-
PAD1	61.4%	78.6%	89.7%	87.5%	85.4%	-
PAD2	48.7%	47.8%	7.1%	69.7%	70.1%	47.8%**

*These cycles were incomplete and the model for the preceding cycle was used.

**The model for the last cycle in Night 1 was used for these cycles.

Table 5 .

OVERALL RESULTS OF REGRESSION ANALYSIS
FOR NIGHTS 1 & 2

<u>SUBJECT</u>	<u>NIGHT 1</u>	<u>NIGHT 2</u>
SAF	82.9%	52.0%
CHI	80.5%	61.6%
PAD	80.5%	49.7%
FAR	75.0%	60.7%
SCH	73.3%	43.3%
GIL	72.8%	56.3%
MOS	68.2%	56.1%
PHI	64.4%	45.4%
NOR	60.8%	37.9%

<u>Night</u>	<u>Actual Group</u>		<u>Classification</u>		<u>Nightly Overall Percent Accuracy</u>
	<u>Group</u>	<u>N</u>	<u>REM⁺</u>	<u>NREM</u>	
1	REM ⁺	115	82	33	88.6%
	NREM	298	14	284	
2	REM ⁺	111	80	31	89.2%
	NREM	259	9	250	
3	REM ⁺	134	103	31	88.7%
	NREM	299	18	281	
6	REM ⁺	109	71	38	86.2%
	NREM	275	15	260	
7	REM ⁺	60	59	1	87.3%
	NREM	160	14	146	

TABLE 7

Classification by Group and by Night for Stages REM⁺
(0, 1 and REM combined) and NREM (2, 3, and 4 combined).

Subject: LES

<u>Night</u>	<u>Actual Group</u>		<u>Classification</u>		<u>Nightly Overall Percent Accuracy</u>
	<u>Group</u>	<u>N</u>	<u>REM⁺</u>	<u>NREM</u>	
1	REM ⁺	142	110	32	88.1%
	NREM	270	17	253	
2	REM ⁺	104	61	43	84.1%
	NREM	323	25	298	
3	REM ⁺	133	22	111	66.0%
	NREM	296	35	261	
4	REM ⁺	120	89	31	88.1%
	NREM	301	19	282	
5	REM ⁺	160	53	107	60.6%
	NREM	289	70	219	

TABLE 8

Classification by Group and by Night for Stages REM⁺
(0, 1 and REM combined) and NREM (2, 3, and 4 combined).

Subject: FER

<u>Night</u>	<u>Actual Group</u>		<u>Classification</u>		<u>Nightly Overall Percent Accuracy</u>
	<u>Group</u>	<u>N</u>	<u>REM⁺</u>	<u>NREM</u>	
1	REM ⁺	90	66	24	90.9%
	NREM	330	14	316	
2	REM ⁺	88	49	39	87.8%
	NREM	329	12	317	
3	REM ⁺	126	73	53	82.8%
	NREM	299	20	279	
6	REM ⁺	112	70	42	87.0%
	NREM	334	16	318	
7	REM ⁺	98	68	30	79.7%
	NREM	113	17	116	

TABLE 9

Classification by Group and by Night for Stages REM⁺
(0, 1 and REM combined) and NREM (2, 3 and 4 combined).

Subject: OWN

To emphasize and summarize the results of our previous studies which are pertinent to the present research, the following points should be reiterated.

- A. From Welch et al.⁸² we learned that beat-by-beat heart rate does contain sleep information.
- B. From Aldredge et al.¹ we found that (1) average heart rates are not the same throughout the night and that each cycle of sleep has its own norms and can be modeled separately, and (2) that average heart rate during different levels of sleep are significantly different within a given sleep cycle.
- C. From Weber et al.⁸¹ we were provided with a plausible automated technique for separating sleep cycles using beat-by-beat heart rate since a cycle, as we have defined it, begins and ends with the onset of Stage 1/REM.
- D. From Lisenby et al.⁵⁴ we can see that Beatquency domain analysis contains remarkable intra-subject consistencies.
- E. From Lisenby et al.⁵⁶ we found that, although still short of the desired results, Beatquency domain analysis has proven to be a significant improvement over our past efforts and produces results comparable to those obtained by other researchers using other methods of EEG analysis.

CHAPTER IV

METHOD

The development of the composite sleep scoring algorithm involved three phases. These phases were:

- I. Preprocessing of the data base
- II. Development and training of the algorithms
- III. Testing of the algorithms (3 parts)

Phase I

The data base used in this research was the same as that used in our previous study.^{1,54,56,81,82} In all, sleep pattern analog recordings were made on nine normal subjects over two complete nights of sleep for each of nine subjects, on two normal subjects over five nights, and on one subject over six nights, for a total of 34 nights. These recordings were made after "first night effects" had been eliminated. The analog tapes for the first nine subjects, which were recorded in the sleep laboratory at the University of Florida, contained two channels of EOG, eight channels of EEG, and two channels of ECG. In addition the 14-channel magnetic tape contained a slow time code (hours and minutes) and a fast time code (modulated 1 KHz sinusoid). The analog tapes for the other three subjects, which were recorded in the sleep laboratory at the U.S. Navy Research Laboratory in San Diego, contained two channels of EOG, one channel of C_3/A_1-A_2 EEG, one channel of SPR, and one channel of ECG. In addition, the magnetic tape contained a slow time code similar to that cited above. These data were also recorded on continuous paper strip charts which were used in the visual scoring of sleep stages. Each night of the Florida data was hand scored on a minute-by-minute basis by three trained experts working independently and using a modified Dement-Kleitman criteria as outlined in Table 10⁸⁴. The resulting scores, along with subject code and time code, were punched

Table 10

SLEEP SCORING CRITERIA OF ONE MINUTE
EEG EPOCHS

<u>STAGE</u>	<u>DEMENT-KLEITMAN</u>	<u>UNIVERSITY OF FLORIDA</u>
0 (Awake)	No Criteria Stated	Each epoch composed of at least 30 seconds 8 to 12 Hz occipital activity with a minimum amplitude of 20 μ V.
1	a) Absolute lack of spindle activity b) A low voltage, relative fast pattern c) Interrupted alpha activity	Epoch composed of less than 30 seconds of 8 to 12 Hz activity [of 20 μ V occipital activity] and no more than one well defined spindle or k complex (4.5) and less than 12 seconds of delta activity.
2	a) Spindle activity with a low voltage background. b) Certain amount of 3-6 Hz activity c) Occurrence of k complexes d) Less than two 1-2 Hz waves over 100 μ V in 10 seconds (for borderline case with stage 3)	a) Epoch composed of 2 spindles or 2K complexes or one each and no more than 20 seconds [12 seconds] of 1 to 3 Hz. [20 μ V or greater slow waves] b) Same as Stage 1, only more than one K complex or spindle per epoch.
3	a) High voltage slow waves with some spindling superimposed. b) More than two 1-2 Hz waves over 100 μ V in 10 seconds but less than 30 seconds.	Epoch contained at least 13 seconds of 1-3 Hz 20 μ V or higher activity but less than 30 seconds of this activity.
4	At least half of the record dominated by waves of 100 μ V or greater in the 1-2 Hz range or slower.	Epoch contained at least 30 seconds of 1-3 Hz 20 μ V or higher slow waves.
5 (REM)	Stage 1 sleep with REM	Stage 1 EEG plus evidence of rapid eye movements.

on cards for data storage. Inter-rater agreement ranged from 90.00% to 96.34% with an average of 93.01% over the 18 nights of the first nine subjects. U.S. Navy data were scored by the Rechtshaffen-Kales criteria.

At the University of Texas, the ECG data were read from the analog tapes into an analog R-wave detector whose output generated an interrupt within a digital computer. A timing algorithm measured the elapsed time in milliseconds between successive R-waves. These R-to-R intervals times were then stored on digital magnetic tapes for further processing.⁸⁴

The remainder of the preprocessing phase involved a merger of information from the R-to-R interval data set and the hand scores. Details of these procedures are described in Appendix A. The result was a composite data set containing the following for each subject:

1. Subject name and analog tape numbers
2. Total number of minutes in the night
3. For each minute:
 - a. Time of night
 - b. Number of R-to-R intervals
 - c. The R-to-R intervals for the minute

Phase II

The first objective of Phase II was to define and develop a REM-NREM classifier algorithm, i.e., the algorithm used to separate sleep cycles based on the method described earlier.

This technique developed by Weber et al.⁸¹ was modified in the following manner. For signature spectra, Weber et al. used only those heart beats associated with actual eye movements and a similar sized sample from the heart beats associated with REM sleep but at a time when the eyes were not moving. This often resulted in very small sample sizes. In this study, however, we decided to use all of the heart beats associated with a full epoch of hand-scored sleep stage. By

doing this we hoped to conform more with the visual scoring and to increase our sample size.

During the test night Weber analyzed sequential 128 beat epochs. Although 128 beats could represent up to two minutes of data (heart rate of 64 per minute) and was variable, some decision process was used to merge hand scores with these epochs. We decided to also conform to this same method.

As in Weber's method, the "digitized" ECG data in terms of R-to-R interval times were first represented in what we call the "Heart Beat Domain", as seen in Fig. 3. The independent variable in this domain was heart beat number occurring in any one minute. The dependent variable was the magnitude of the corresponding R-to-R interval. It should be noted that the data were discrete and equally spaced in this domain. Each epoch was filled to 128 beats in order to facilitate use of our Discrete Fourier Analysis (FFT) routine. Epochs of R-to-R interval data for a known level of sleep were converted to the Heart Beat Domain. Epochs were computed for each of the six possible sleep stages, 0 through 5 (REM). In this way we used only epochs which were pure stage (containing no stage transitions). We felt from previous studies that transition epochs (i.e. epochs containing more than one sleep stage) yielded contamination of data which was difficult to correct for later.

These epochs were then transformed via the Fast Fourier Transform to yield an amplitude spectrogram representative of that known level of sleep (Fig. 5). Only the positive frequencies were considered, therefore yielding a 64-point transform with a 65th point serving as the folding frequency³⁴. Since this transform was made via the Heart Beat Domain, we chose to call the transformation space the "Beatquency Domain". Rather than cycles/second as in the conventional frequency domain, our Beatquency Domain was expressed in terms of cycles/beat. We chose not to "normalize" the amplitude of each spectrum so as to take advantage of

the natural difference in amplitude between stages. We then formed two average spectra, REM⁺ (combined stages 0, 1, and 5) and NREM (combined stages 2, 3, and 4). We then smoothed both templates with a three point average technique.

The training of the REM-NREM classifier was done by formulating the template or typical REM and NREM spectra from the data during Night 1 for a combination of two subjects, LES and FER (Fig. 6). Then these templates were used to classify the two subjects' Night 1 into its REM and NREM components as outlined in Fig. 7. The original six stage spectra are shown in Figures 8 through 13. The two templates can be seen in Figures 14 and 15. Figures 16 through 37 illustrate transition epochs which were not used.

It should be explained that preliminary tests were performed to determine how spectra of the separate stages (Stages 0,1,2,3,4,5) differed morphologically. It was found that the spectra distinctly fell into two groups: Stages 0, 1, 5 and Stages 2, 3, 4. It has been our standard procedure to combine Stages 1 and 5 as REM sleep and Stages 2,3, and 4 as NREM sleep. However, Stage 0 or awake was also essentially indistinguishable from Stages 1 and 5. It is known that these stages are similar in many respects.^{4,8,13,75} In fact, Larsen et al.⁵¹ reported the same grouping phenomena with regard to certain EEG measures. Since inspection of the hand scores implied that long periods of arousal were usually closely associated with the cyclic pattern, Stage 0 was incorporated into the definition of REM. This appeared justifiable since the purpose of this procedure is to determine the cyclic pattern rather than distinguish the component levels of sleep.

Phase III - Part 1

The first part of Phase III was the testing of the REM-NREM classification model trained in Phase II. The testing procedure was to use

TRAINING

STEP 1:

REM DATA
COMBINED STAGES 0,1,5



BEATQUENCY
DOMAIN



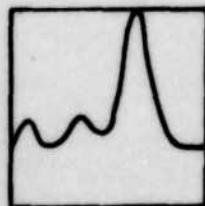
REM TEMPLATE

STEP 2:

NREM DATA
COMBINED STAGES 2,3,4



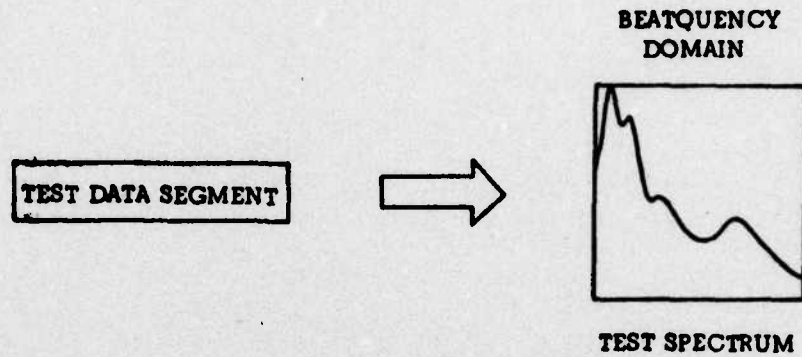
BEATQUENCY
DOMAIN



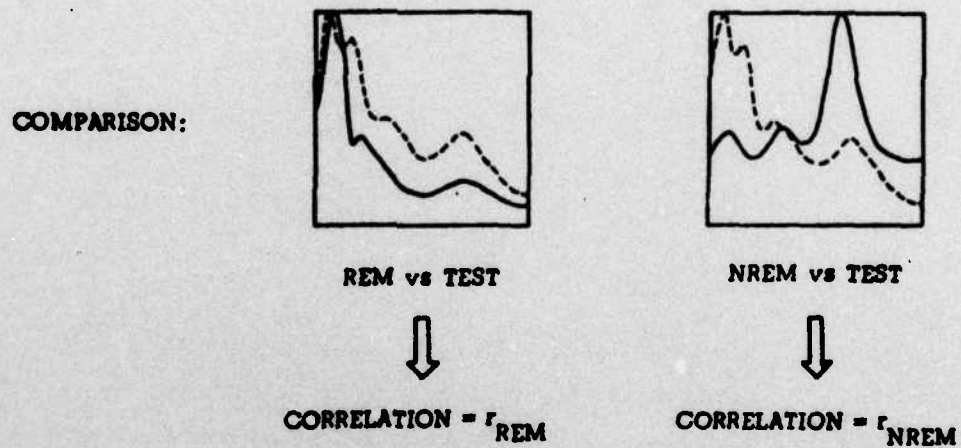
NREM TEMPLATE

Figure 6

STEP 1:



STEP 2:



STEP 3:

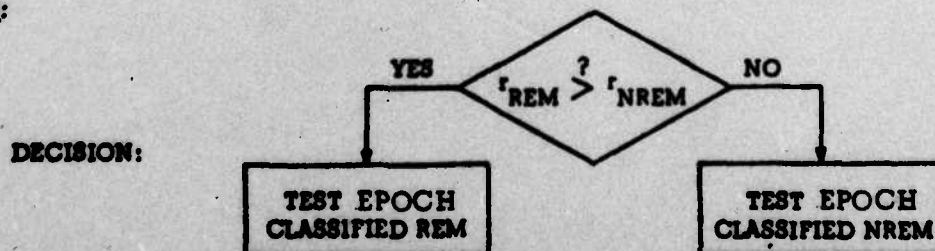


Figure 7

LES-FER STAGE AWAKE

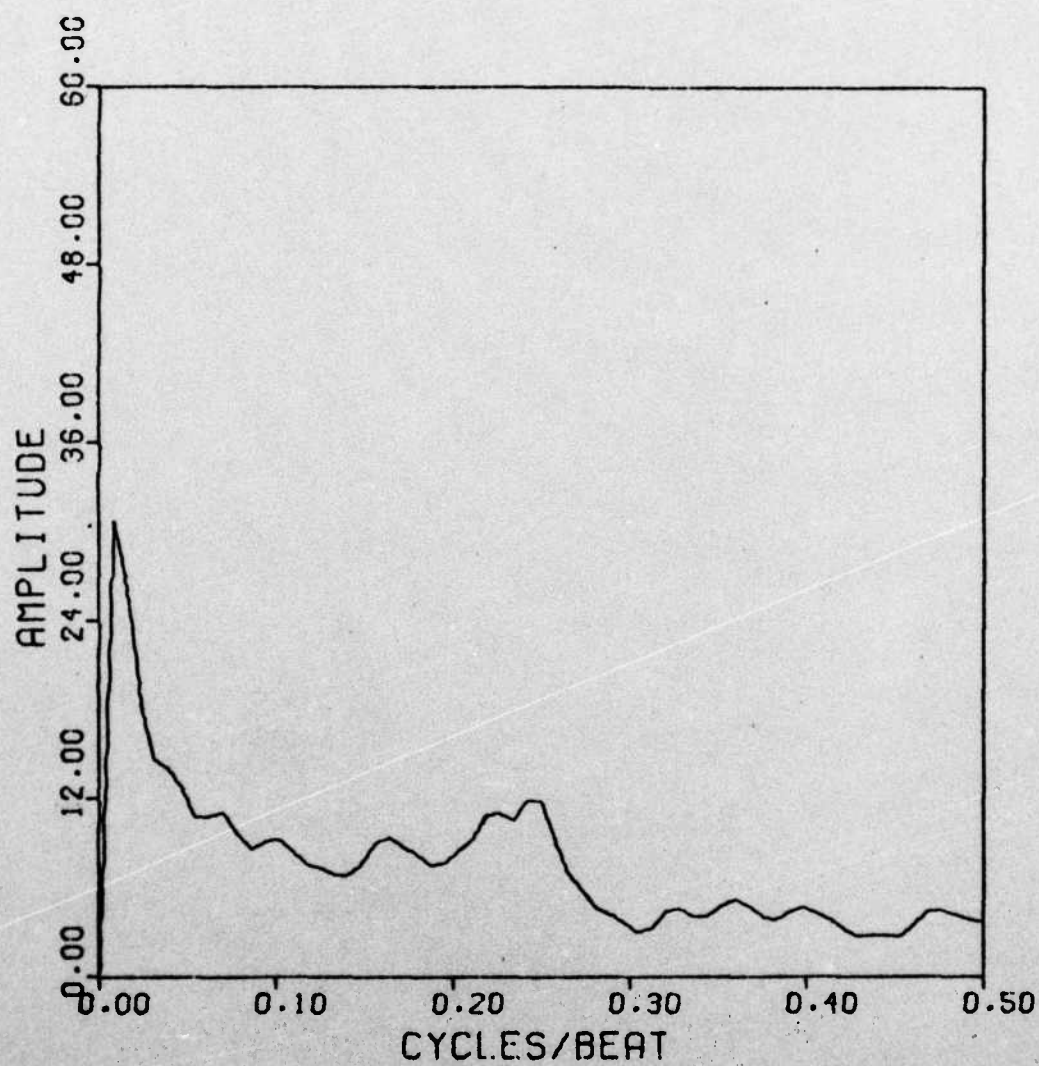


Figure 8

LES-FER STAGE ONE

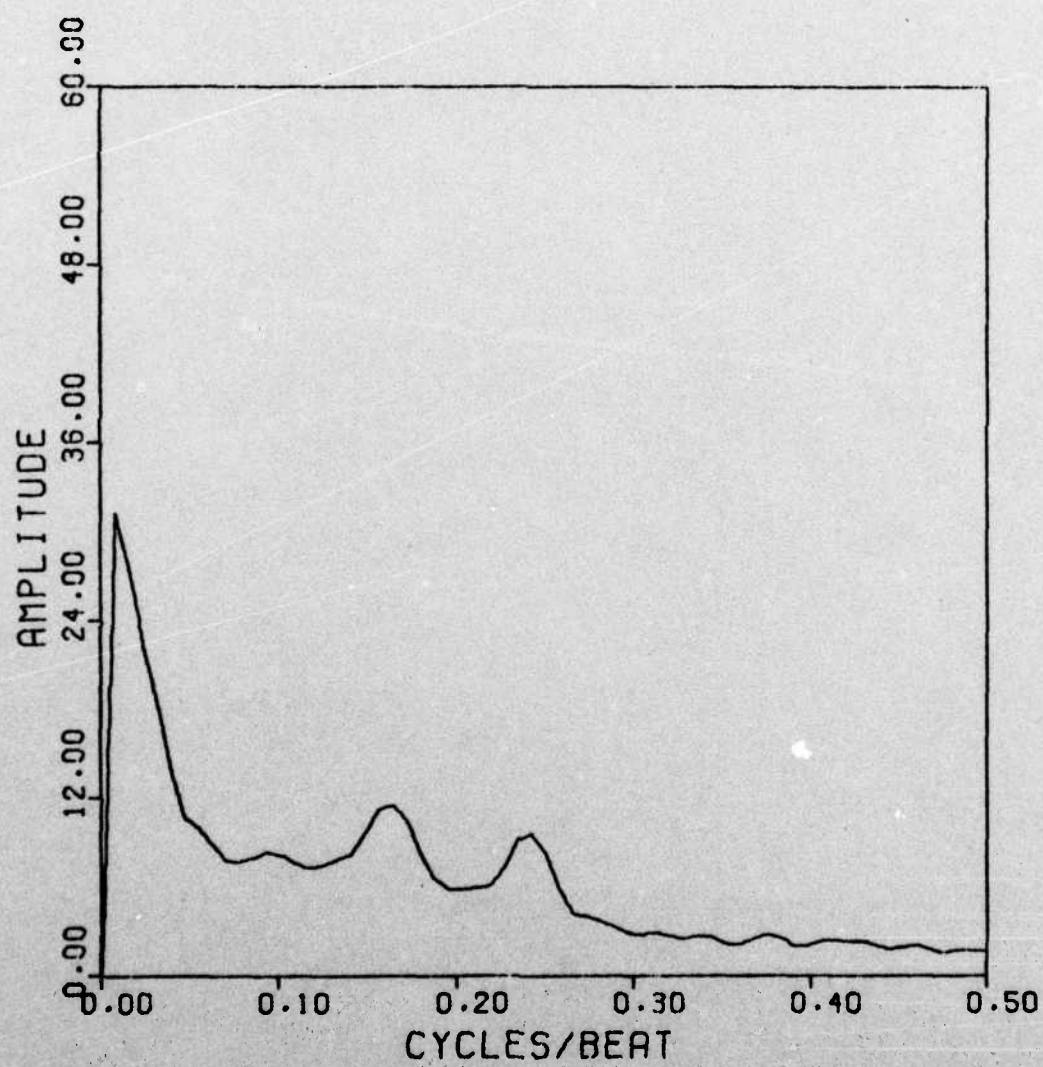


Figure 9

LES-FER STAGE TWO

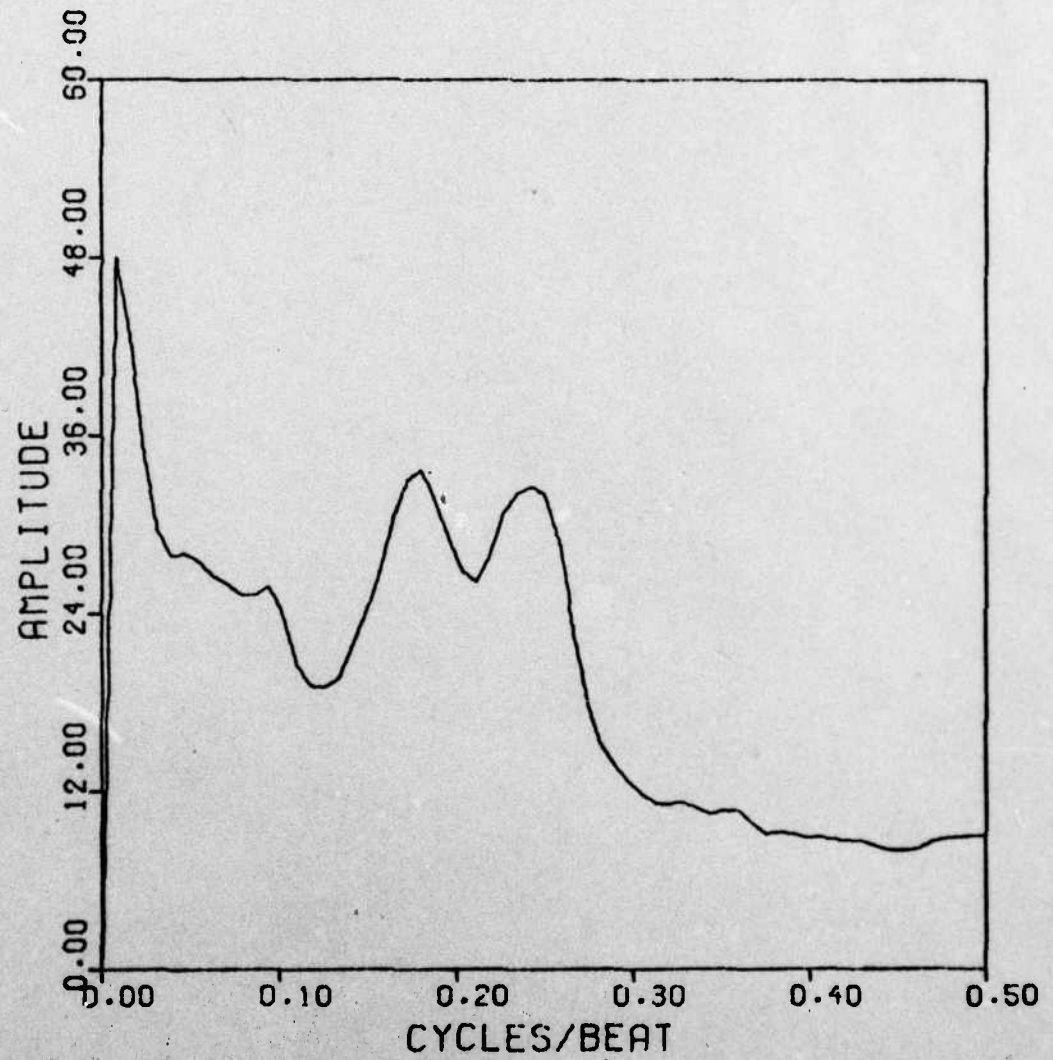


Figure 10

LES-FER STAGE THREE

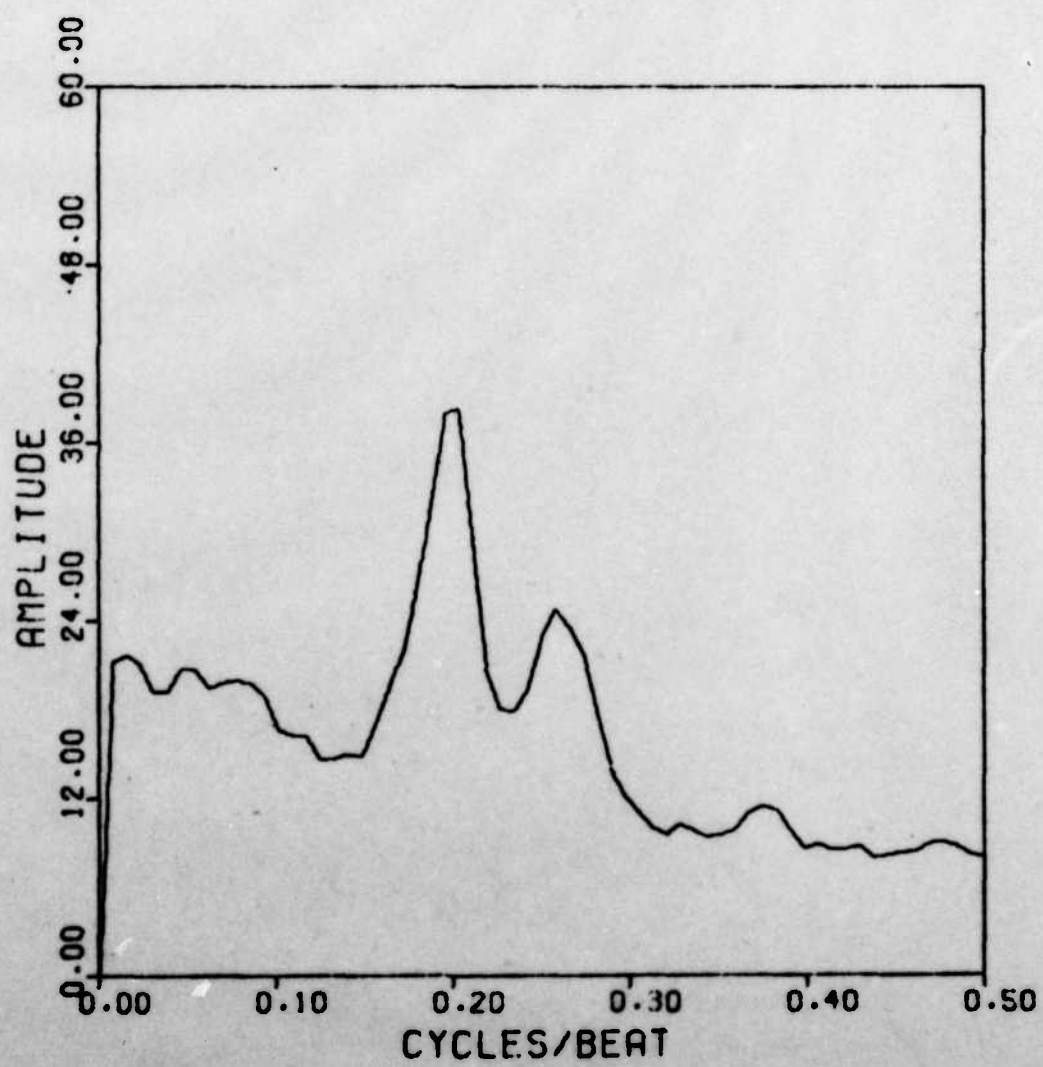


Figure 11

LES-FER STAGE FOUR

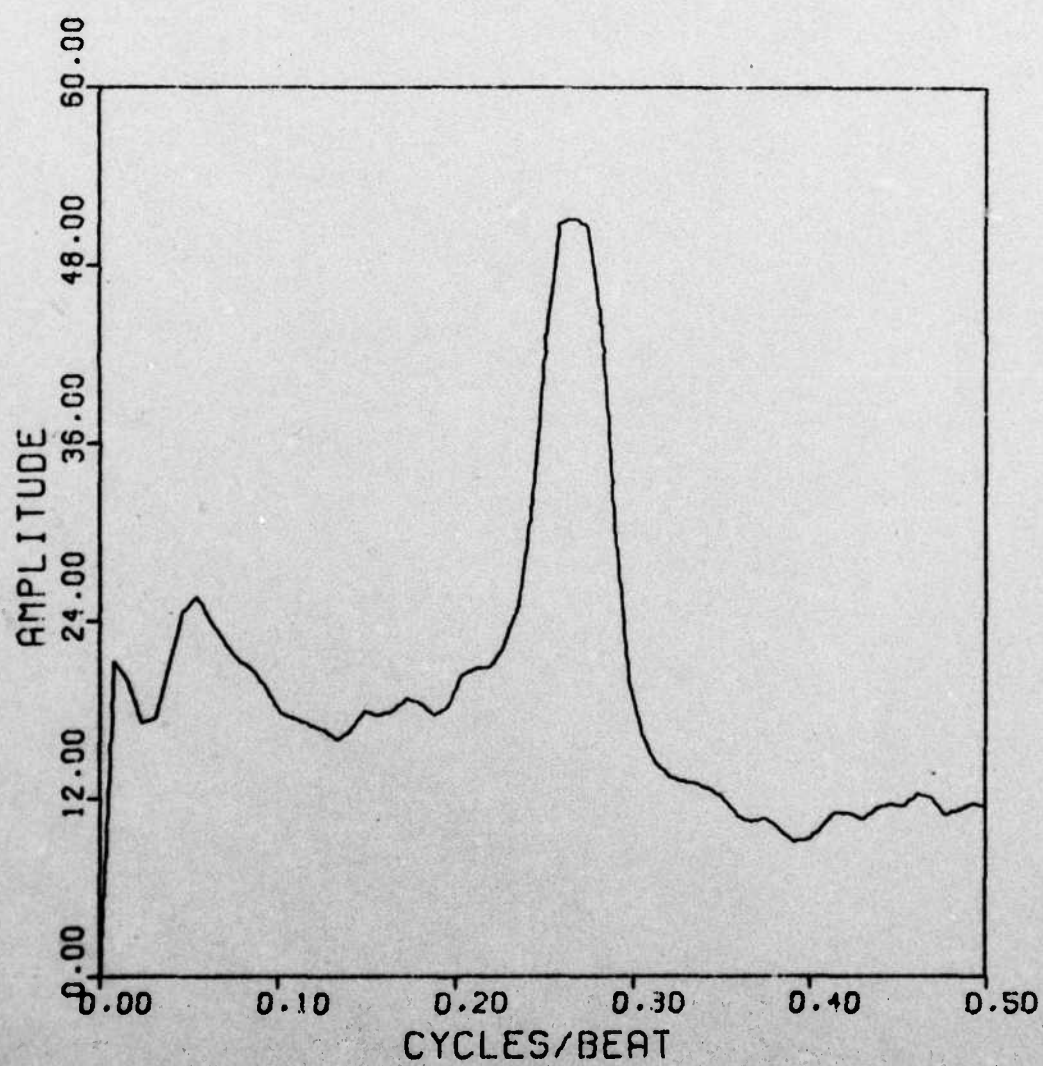


Figure 12

LES-FER STAGE FIVE

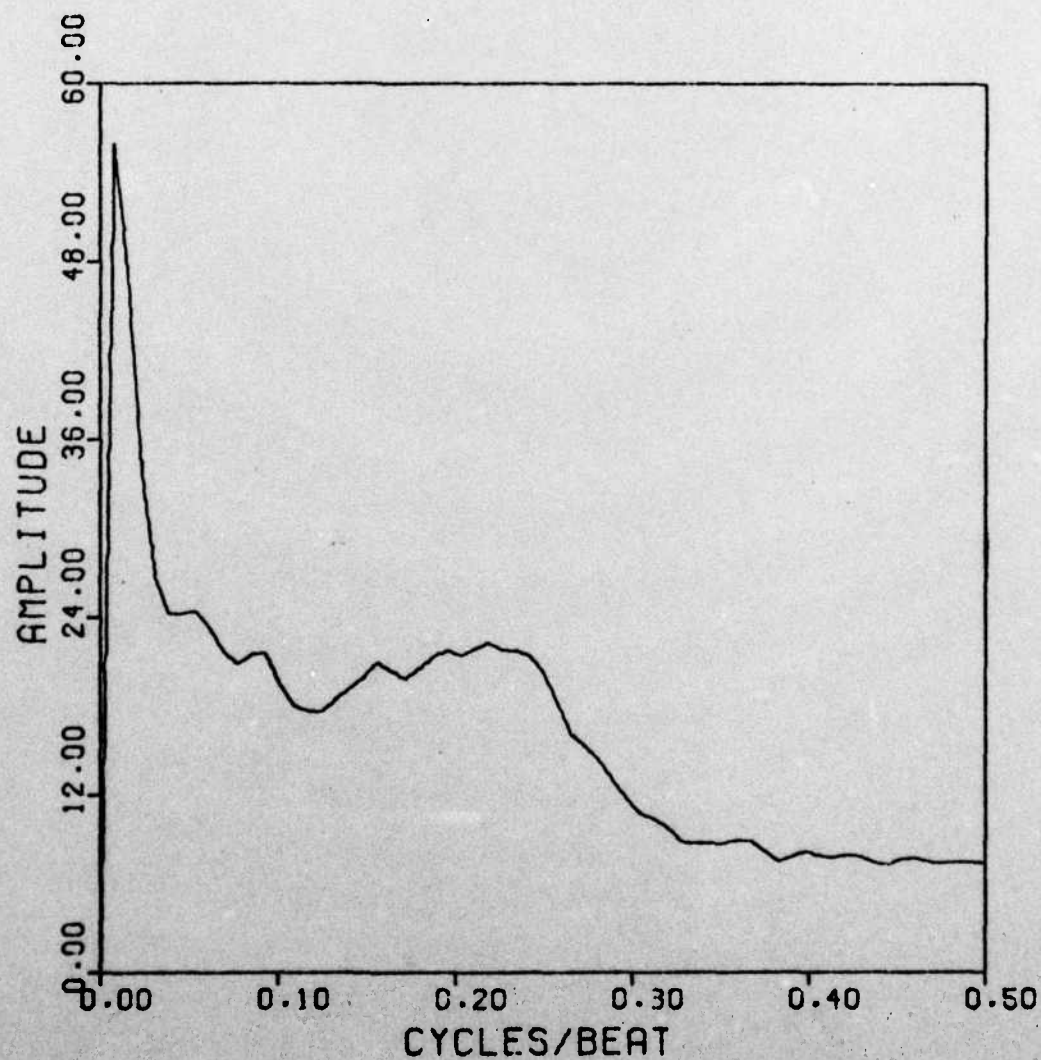


Figure 13

LES-FER REM+ SPECTRA

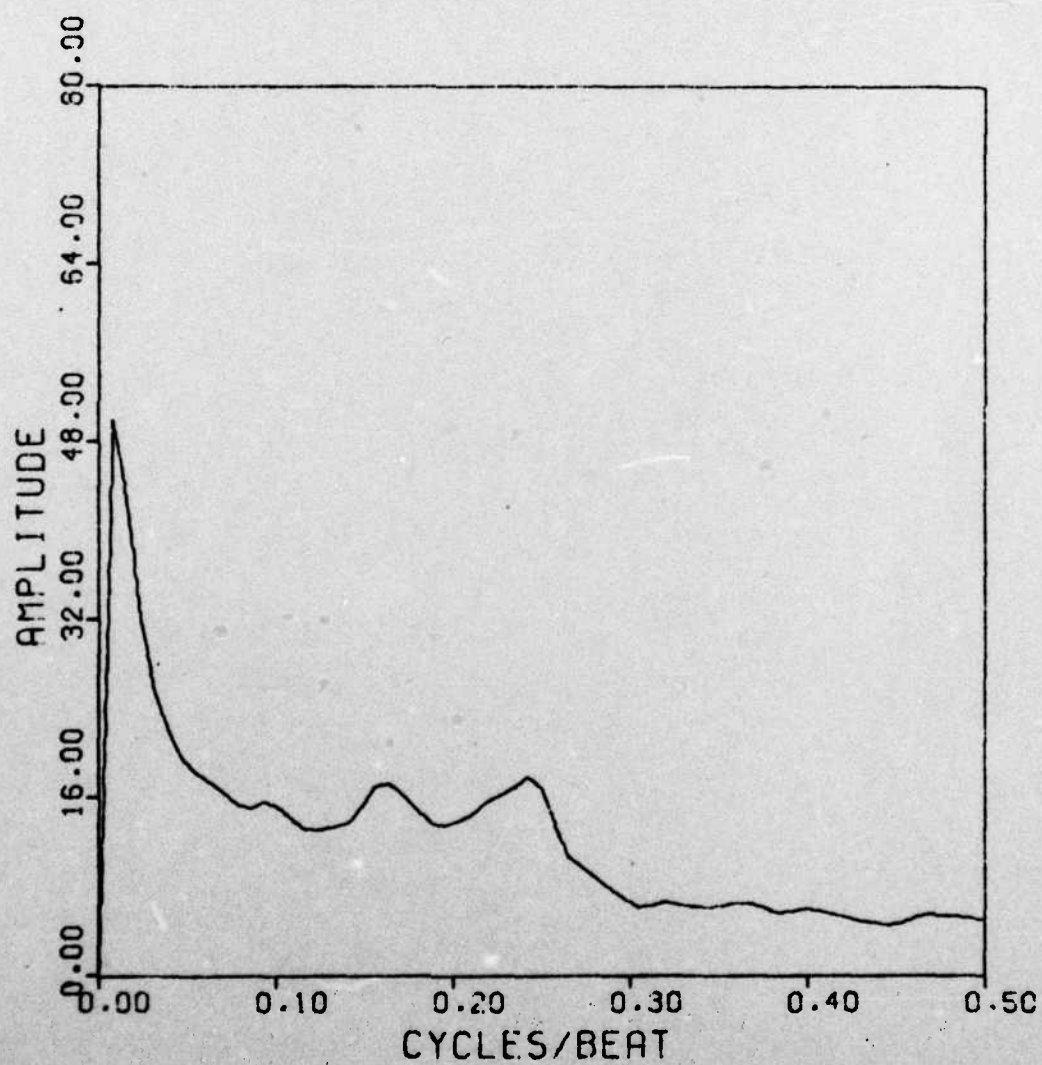


Figure 14

LES-FER NREM SPECTRA

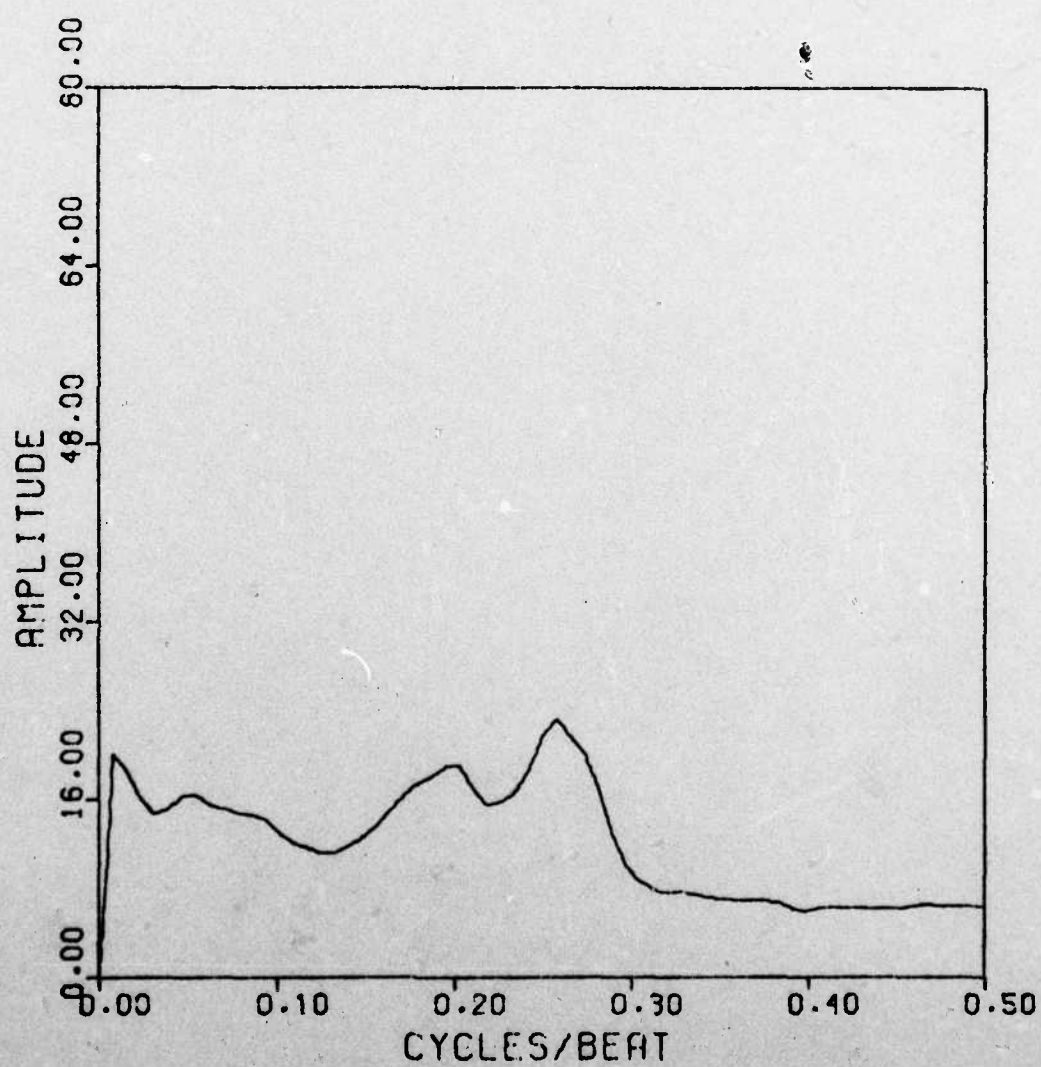
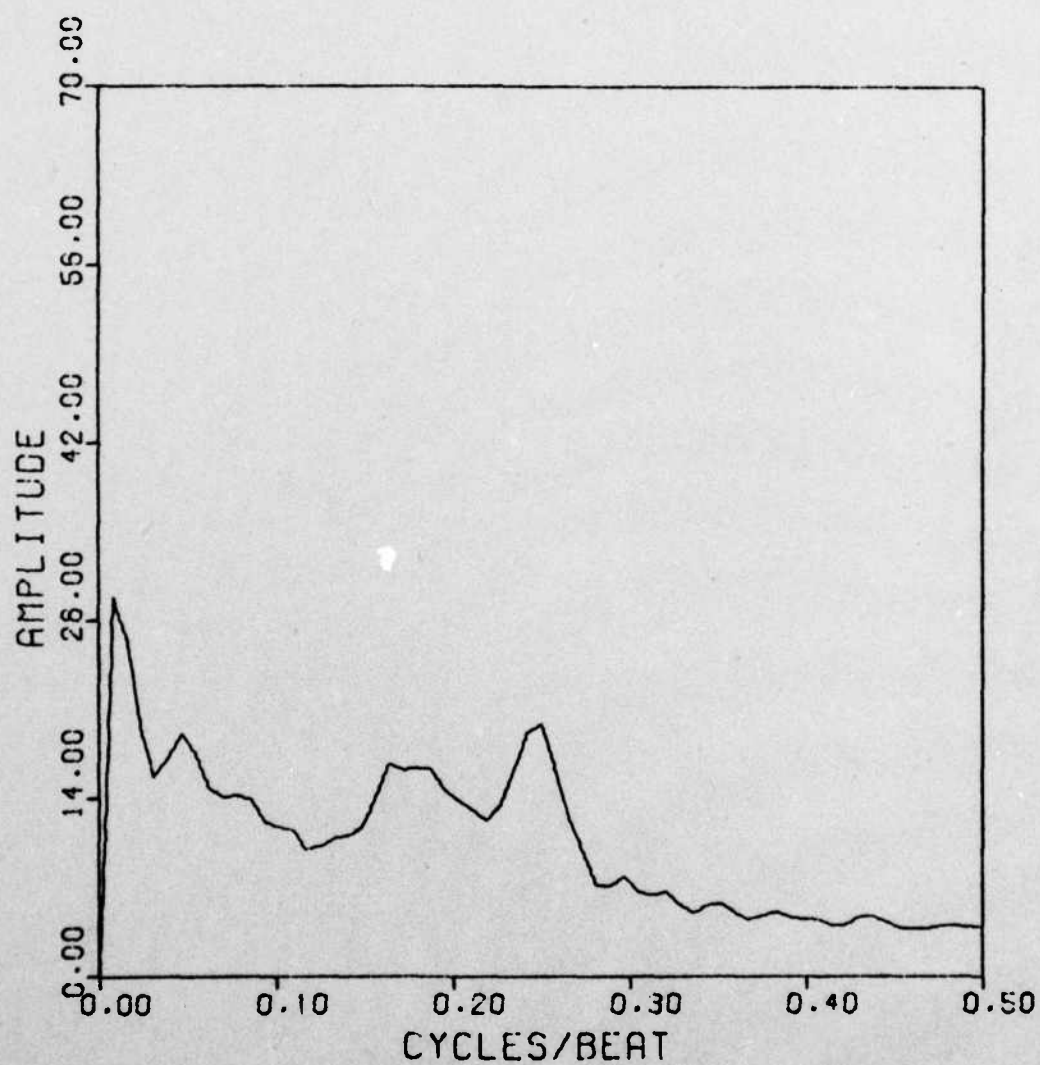


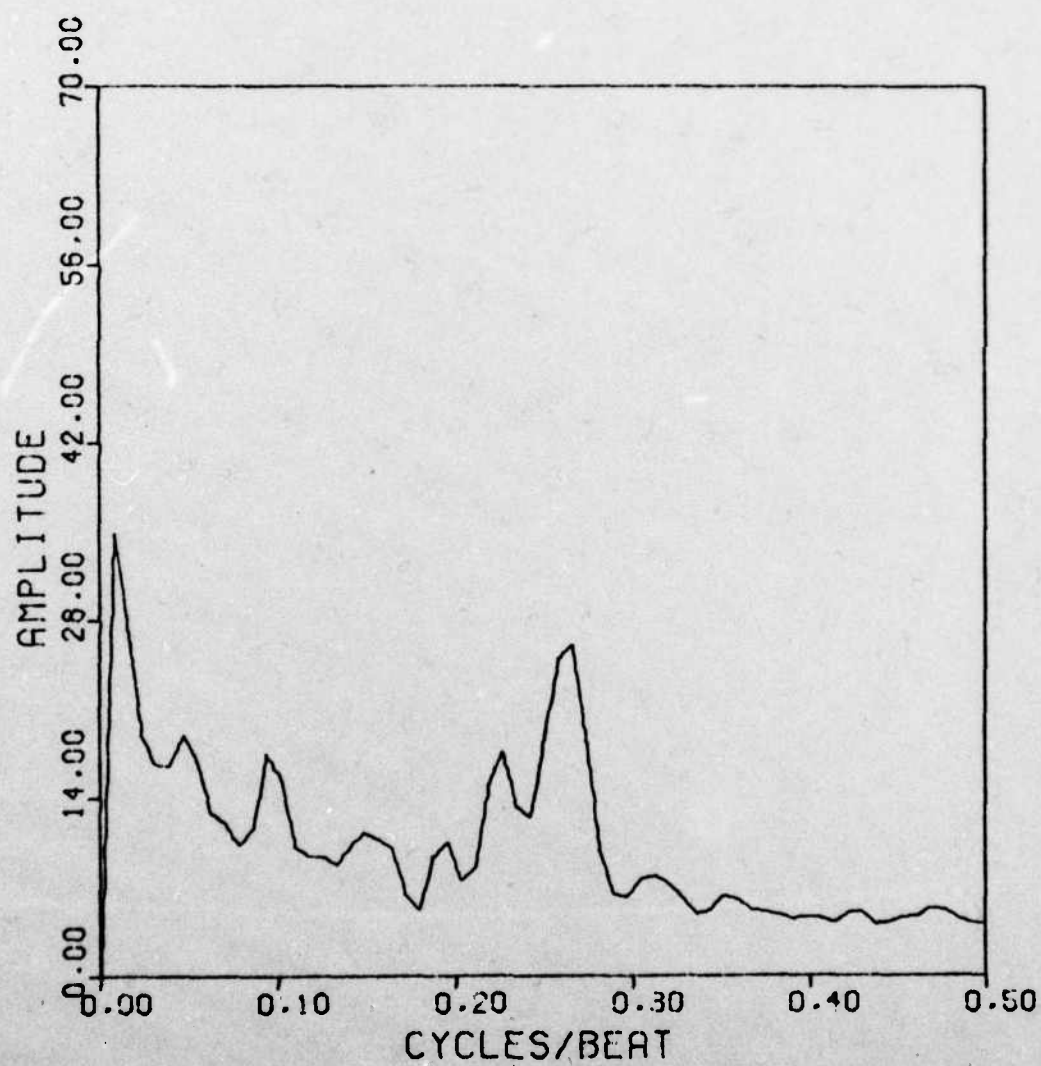
Figure 15

LES-OWN-FER
NIGHTS 1.2
STAGES 0-1



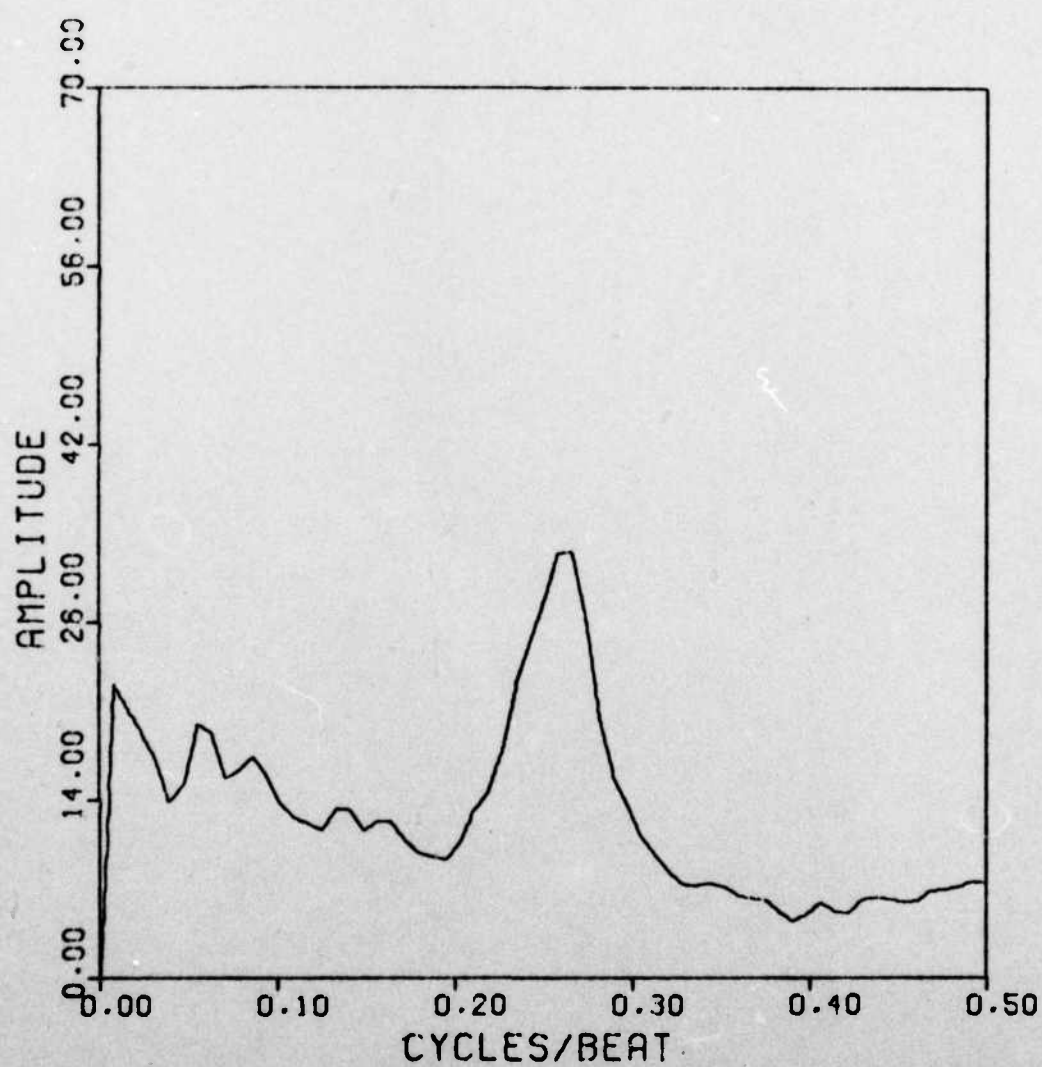
Transition Epoch
Figure 16

LES-OWN-FER
NIGHTS 1,2
STAGES 0-2



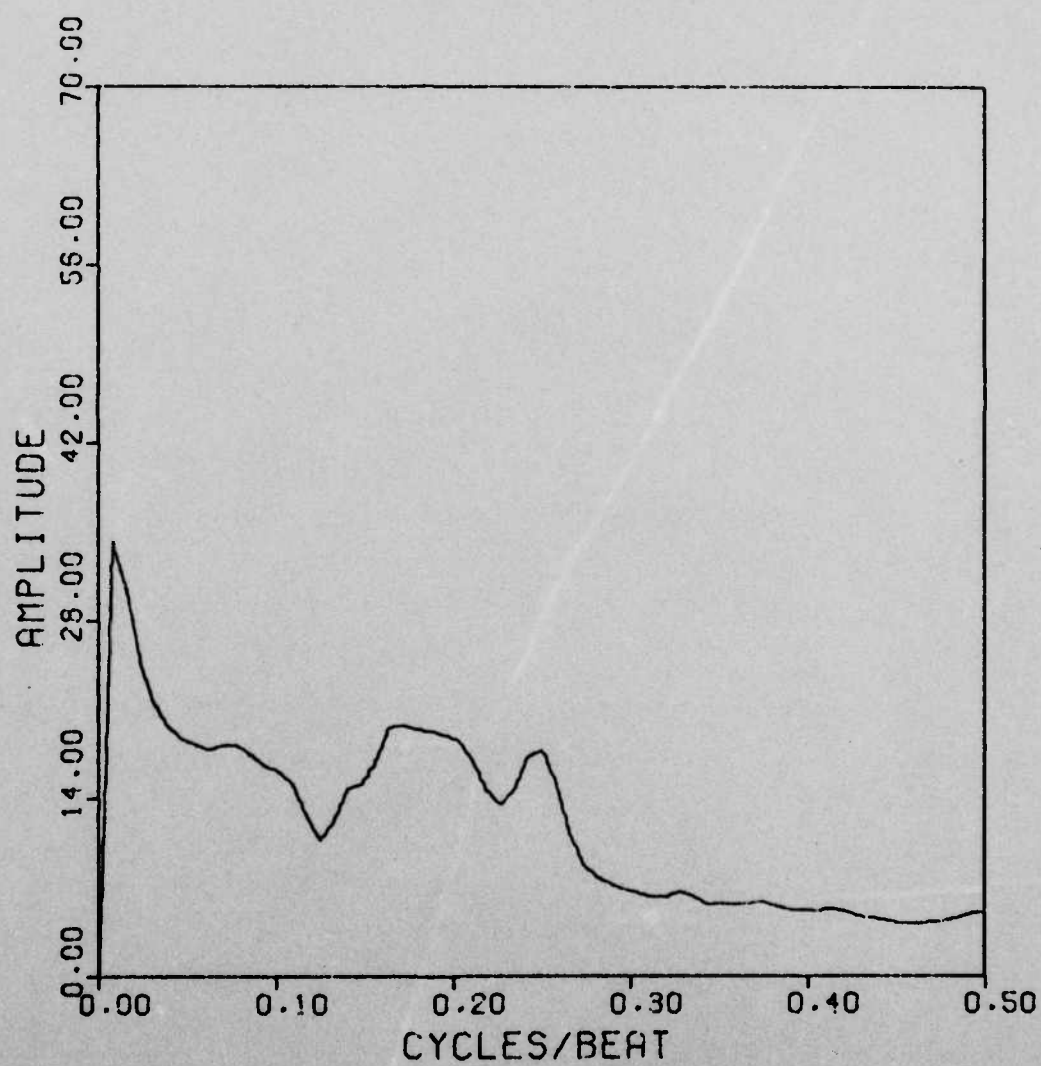
Transition Epoch
Figure 17

LES-OWN-FER
NIGHTS 1,2
STAGES 1-0



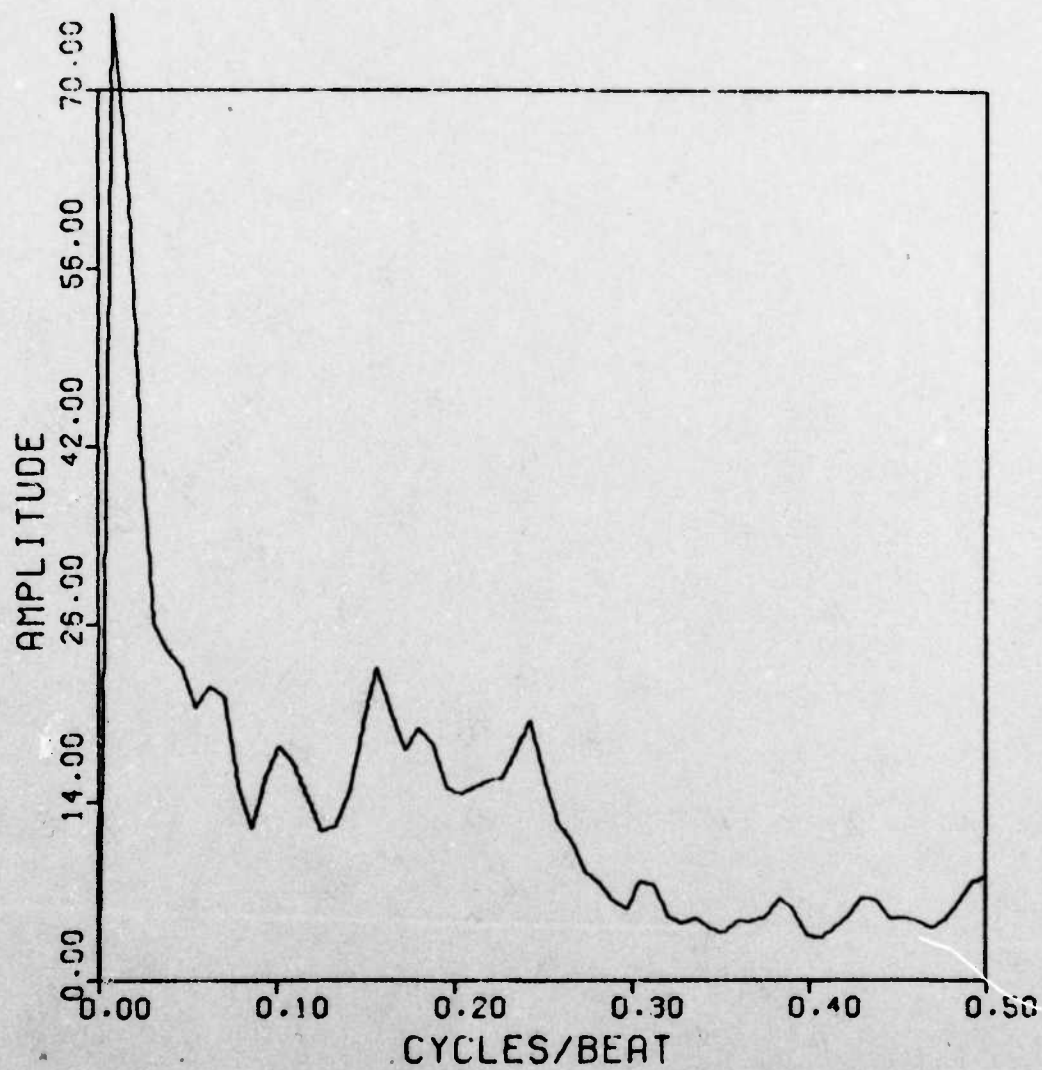
Transition Epoch
Figure 18

LES-OWN-FER
NIGHTS 1,2
STAGES 1-2



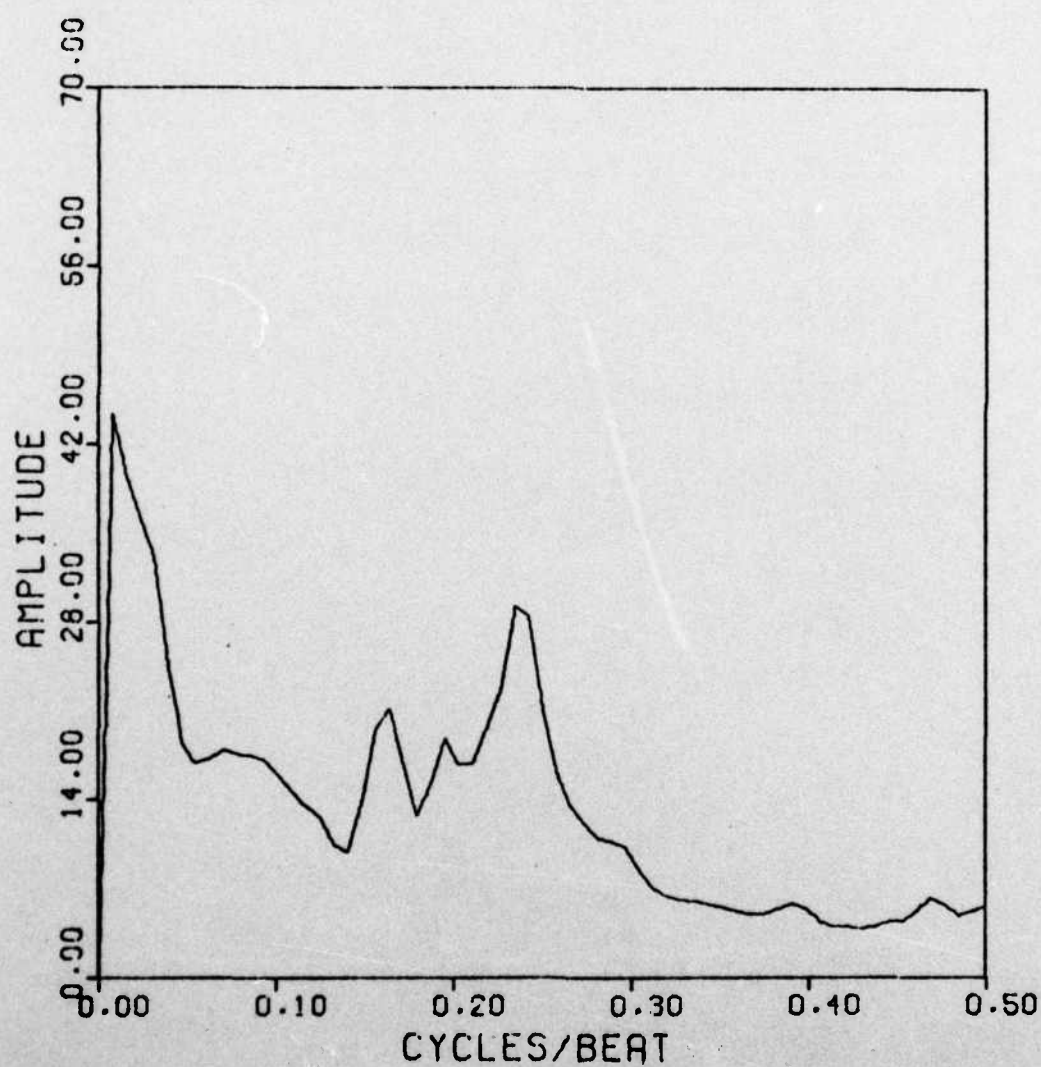
Transition Epoch
Figure 19

LES-OWN-FER
NIGHTS 1.2
STAGES 1-5



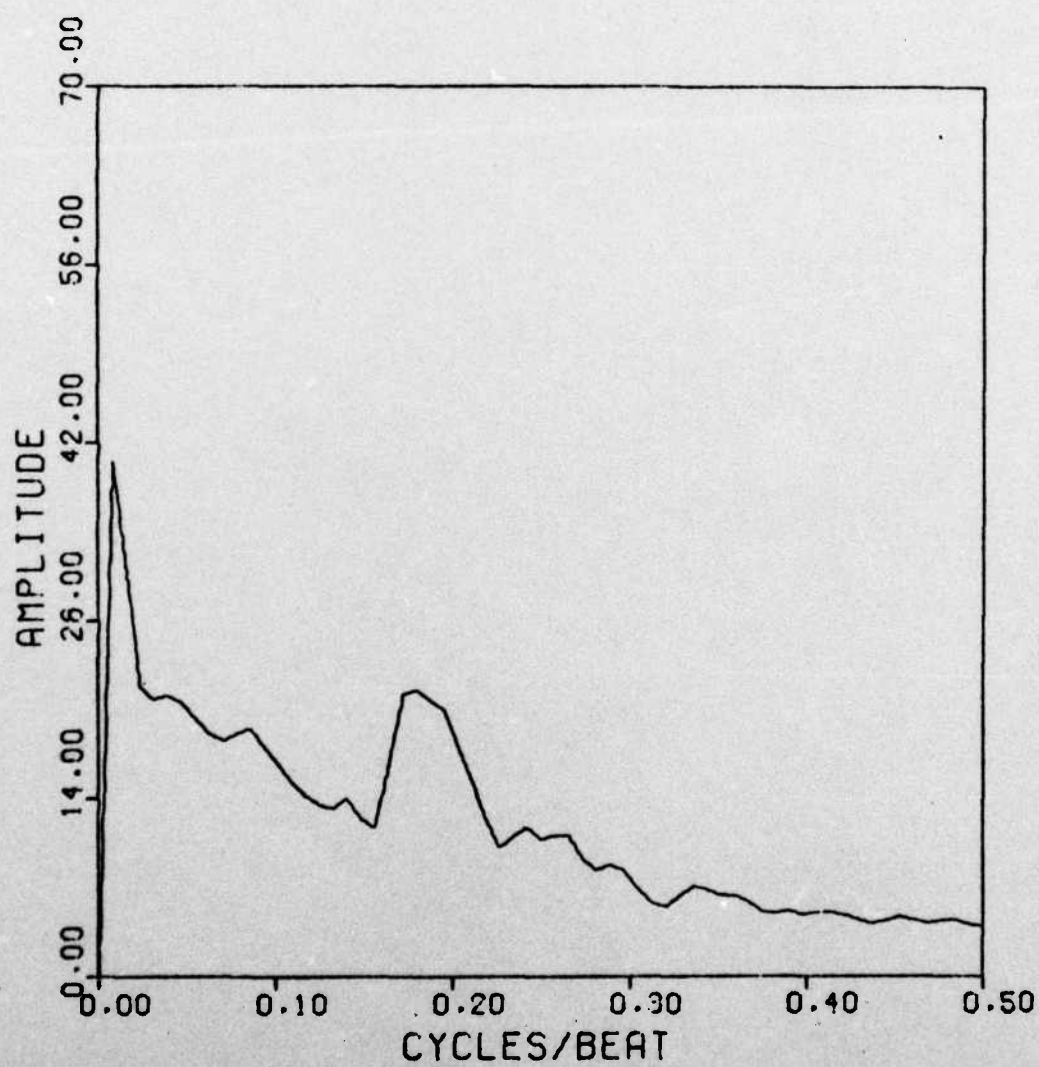
Transition Epoch
Figure 20

LES-OWN-FER
NIGHTS 1.2
STAGES 2-0



Transition Epoch
Figure 21

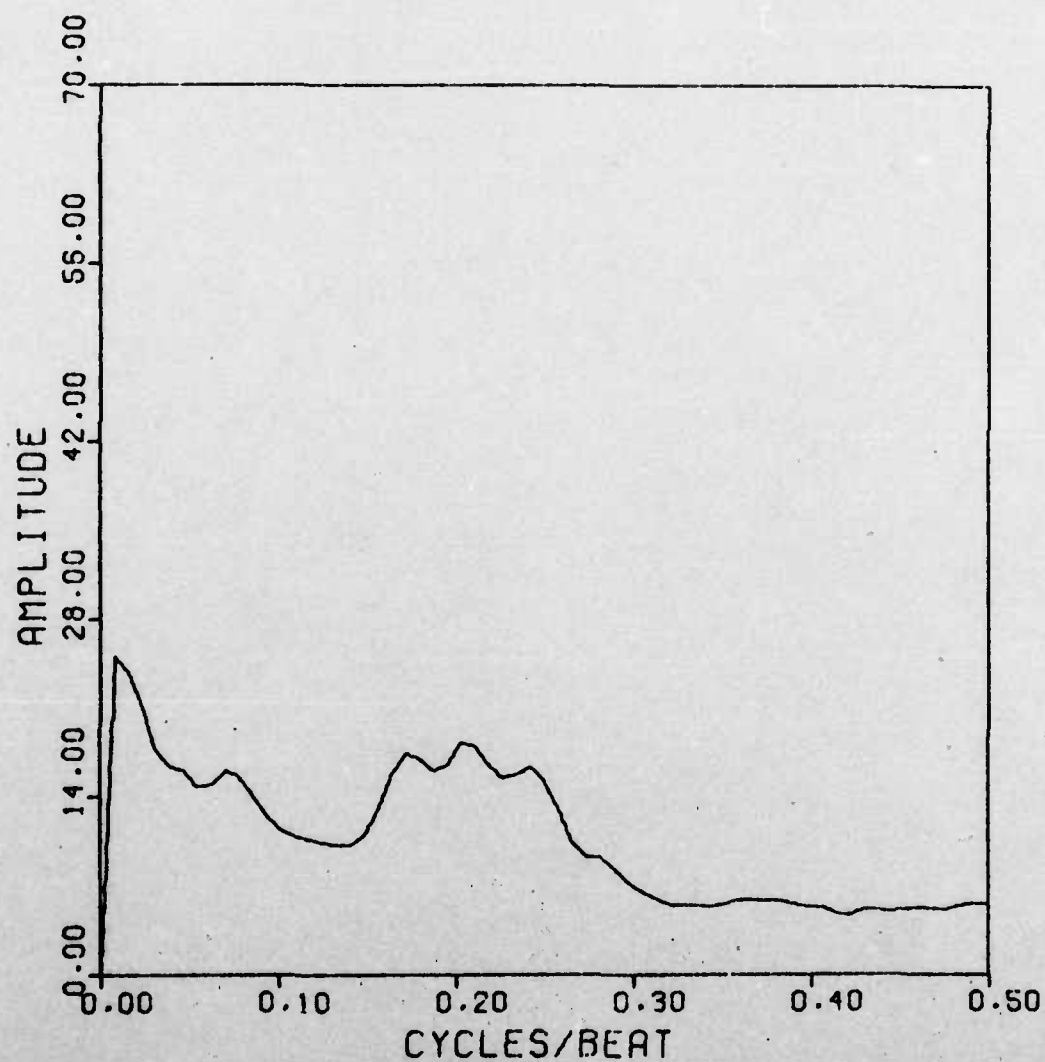
LES-OWN-FER
NIGHTS 1,2
STAGES 2-1



Transition Epoch

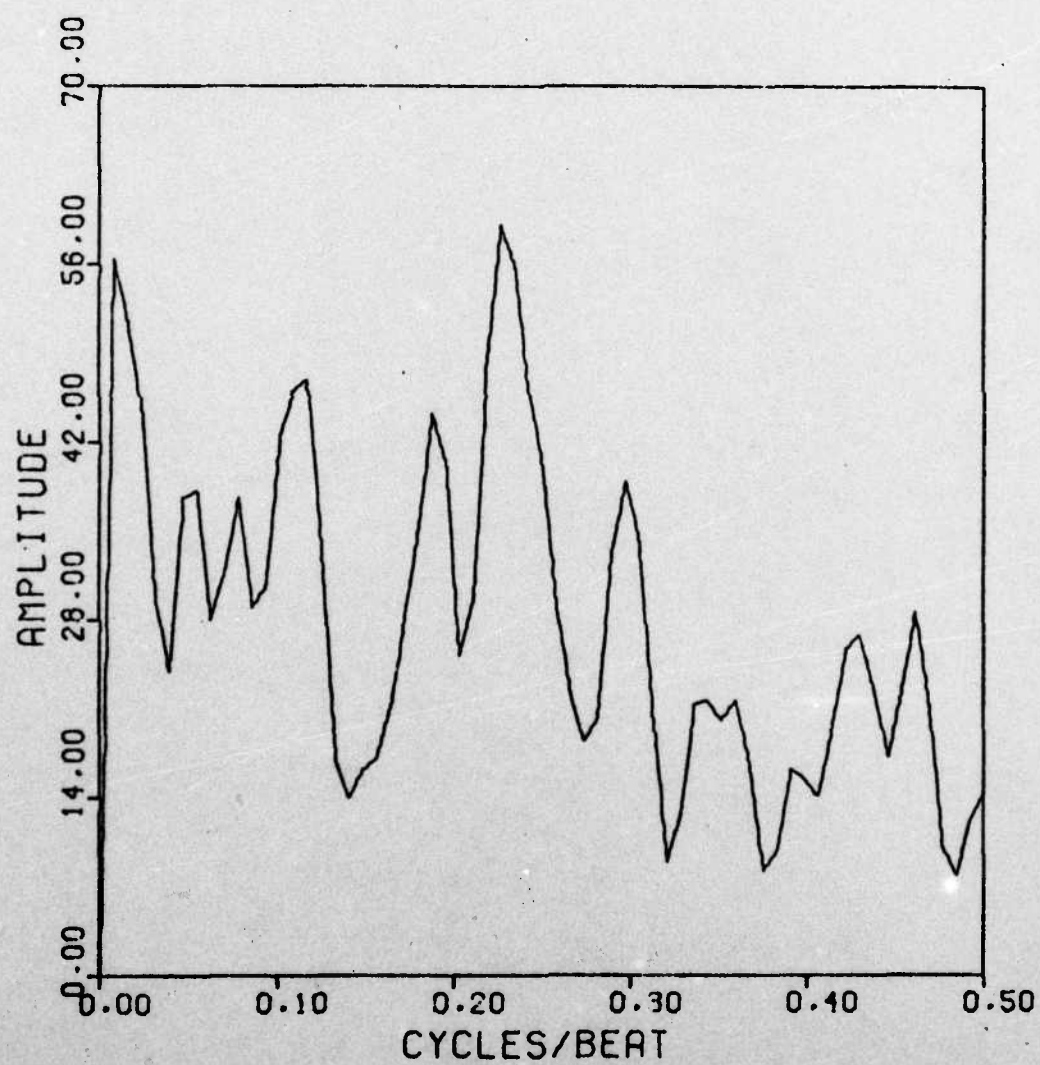
Figure 22

LES-OWN-FER
NIGHTS 1.2
STAGES 2-3



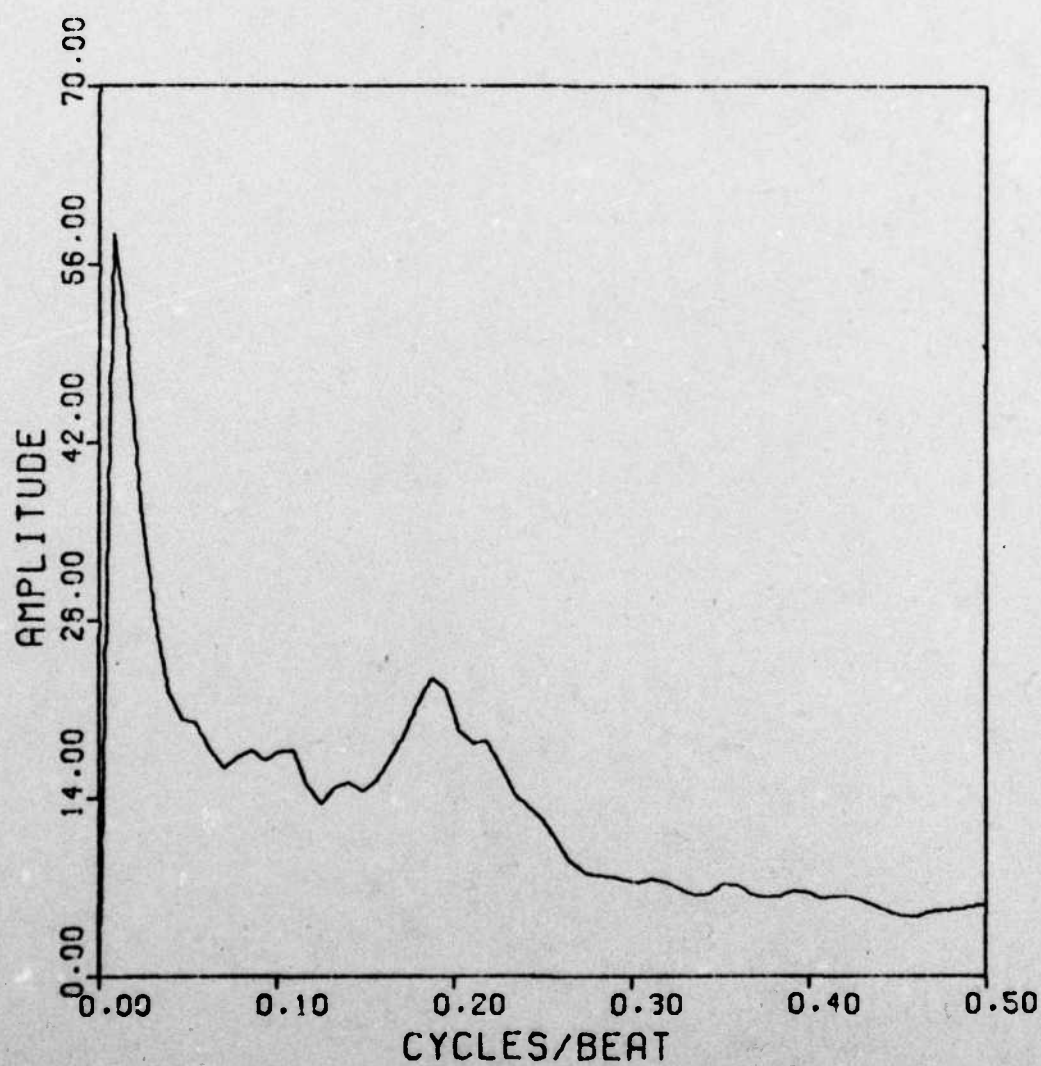
Transition Epoch
Figure 23

LES-OWN-FER
NIGHTS 1,2
STAGES 2-4



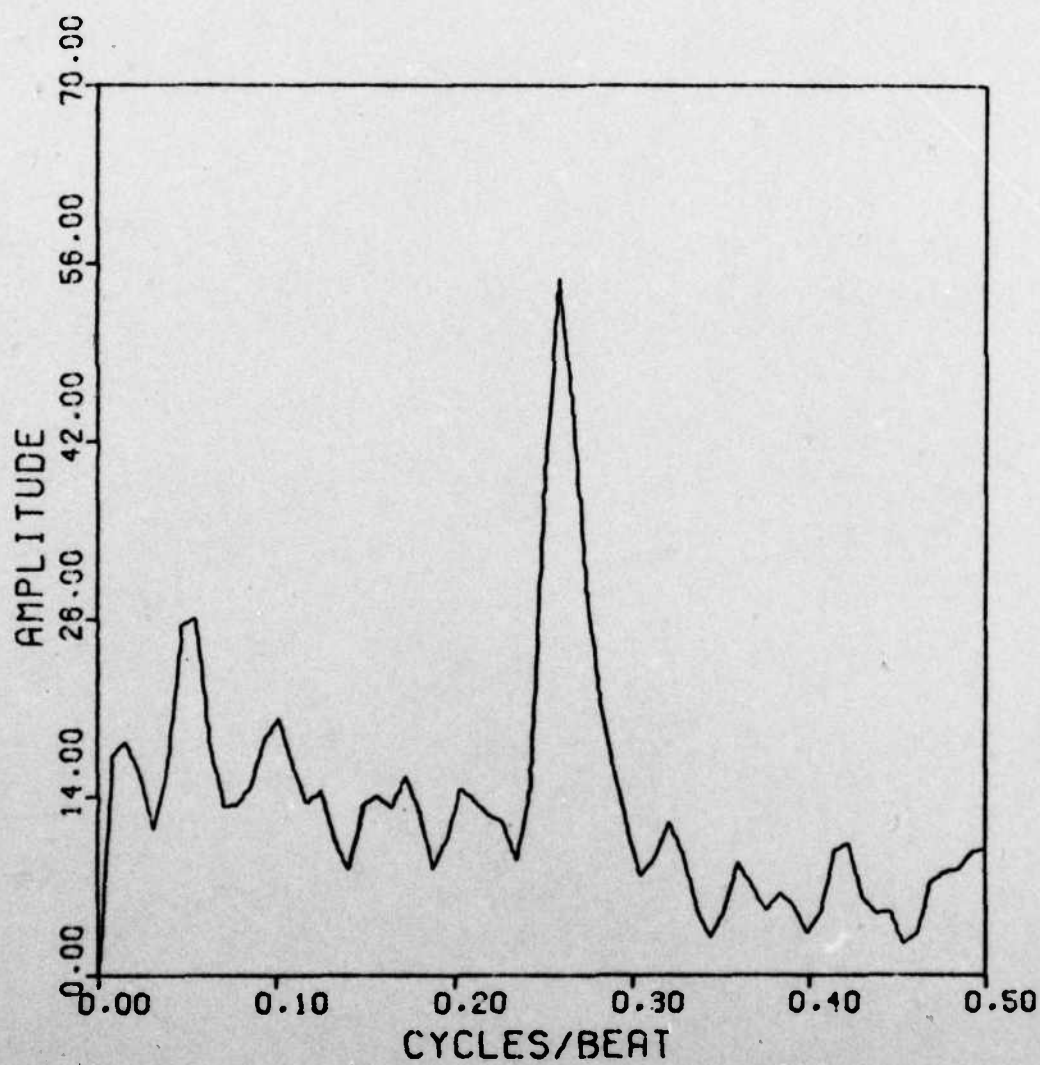
Transition Epoch
Figure 24

LES-OWN-FER
NIGHTS 1,2
STAGES 2-5



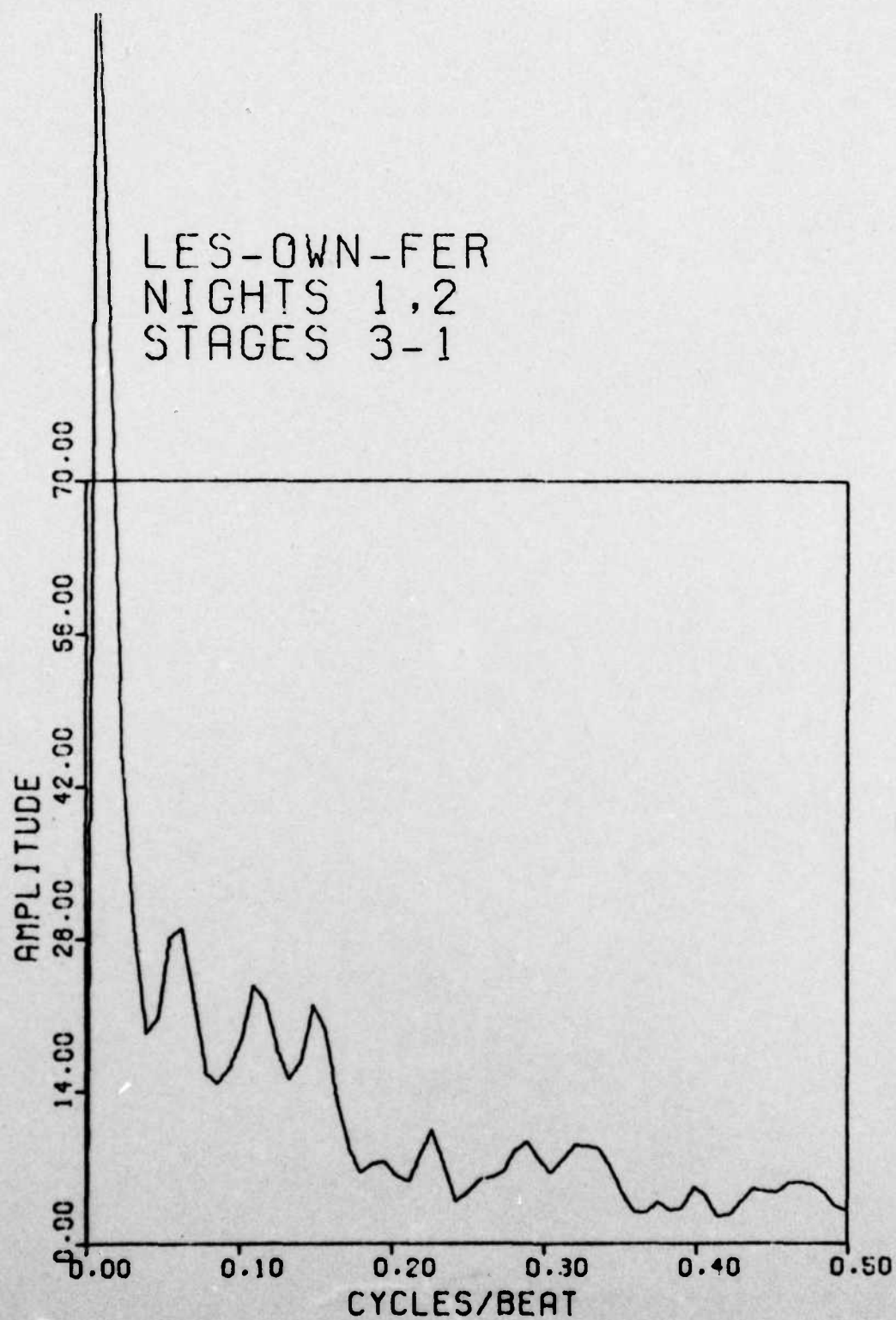
Transition Epoch
Figure 25

LES-OWN-FER
NIGHTS 1,2
STAGES 3-0



Transition Epoch

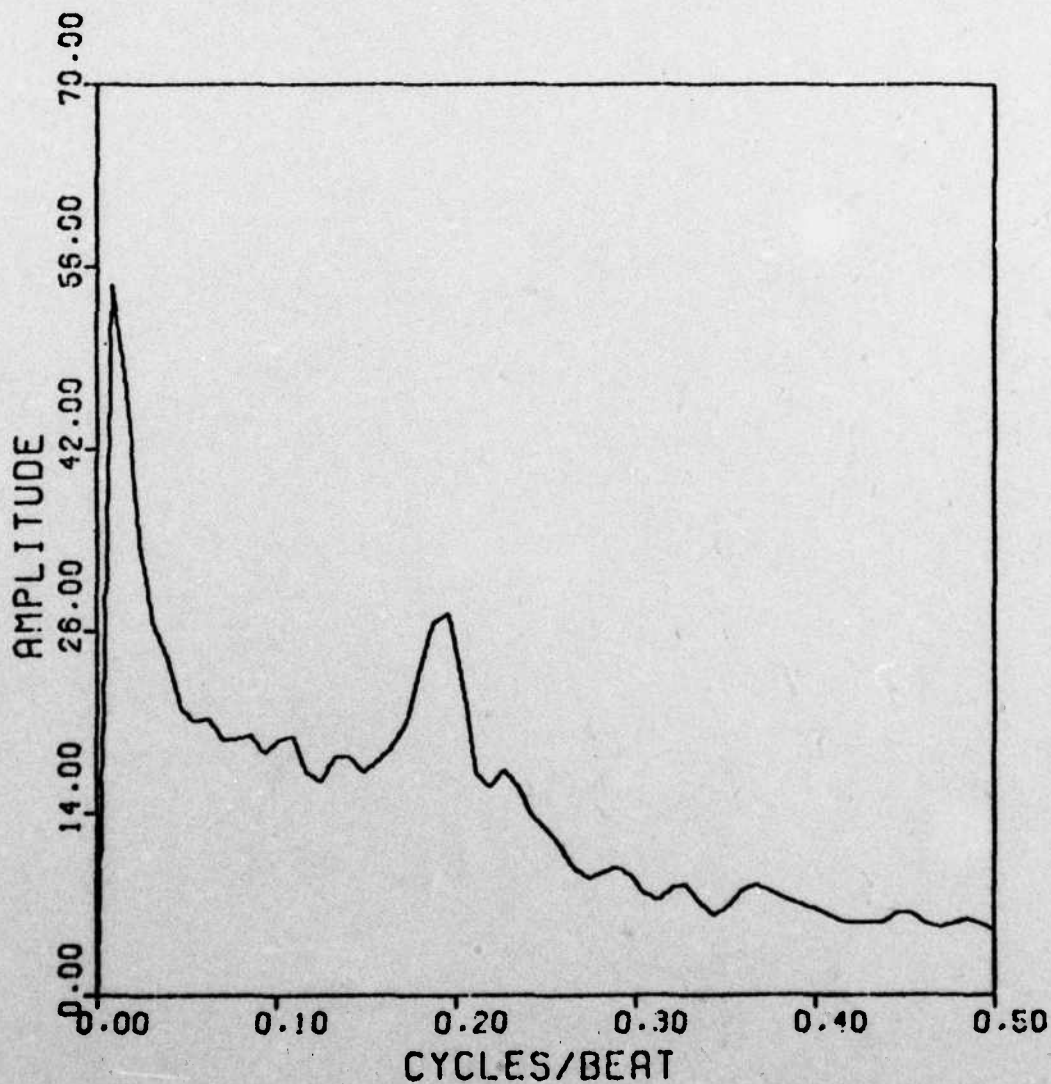
Figure 26



Transition Epoch

Figure 27

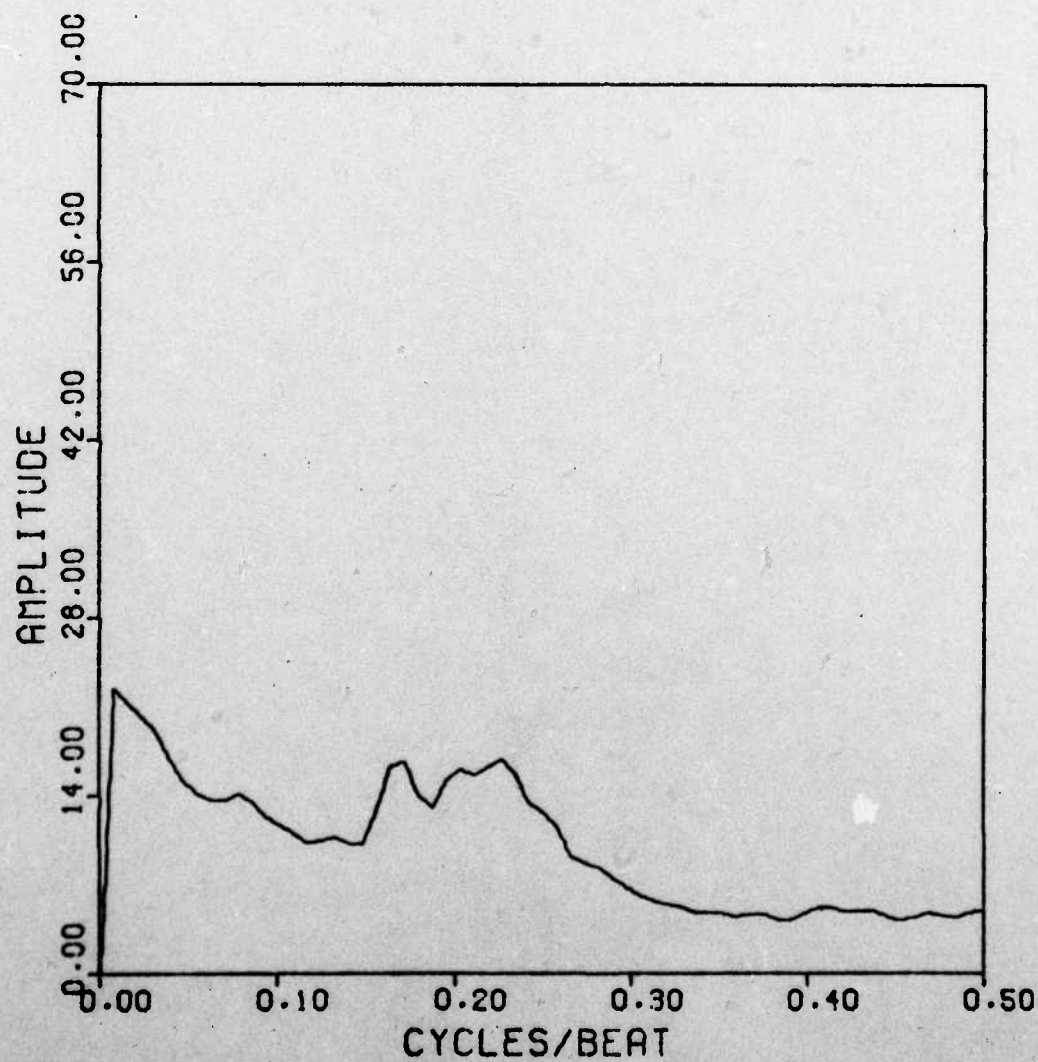
LES-OWN-FER
NIGHTS 1,2
STAGES 3-2.



Transition Epoch

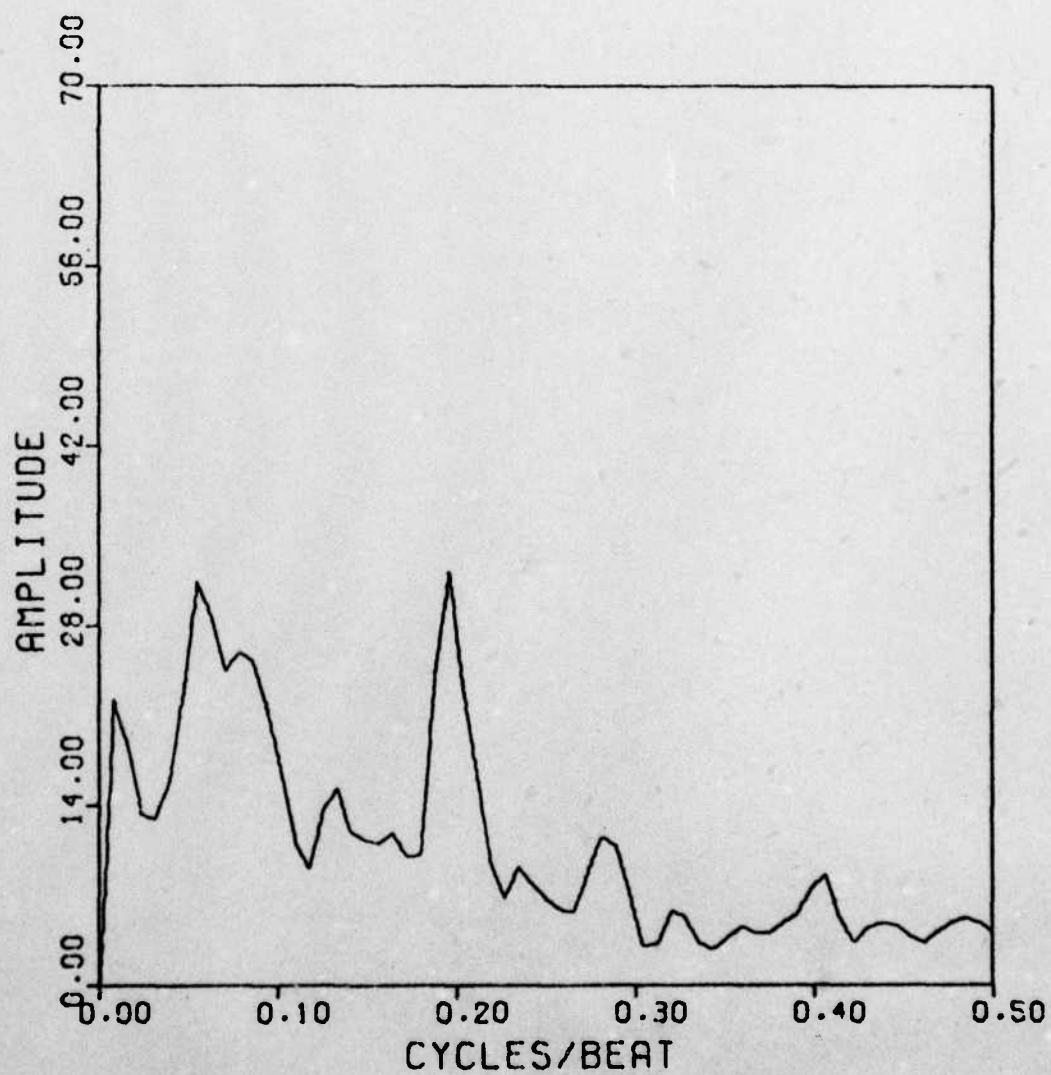
Figure 28

LES-OWN-FER
NIGHTS 1,2
STAGES 3-4



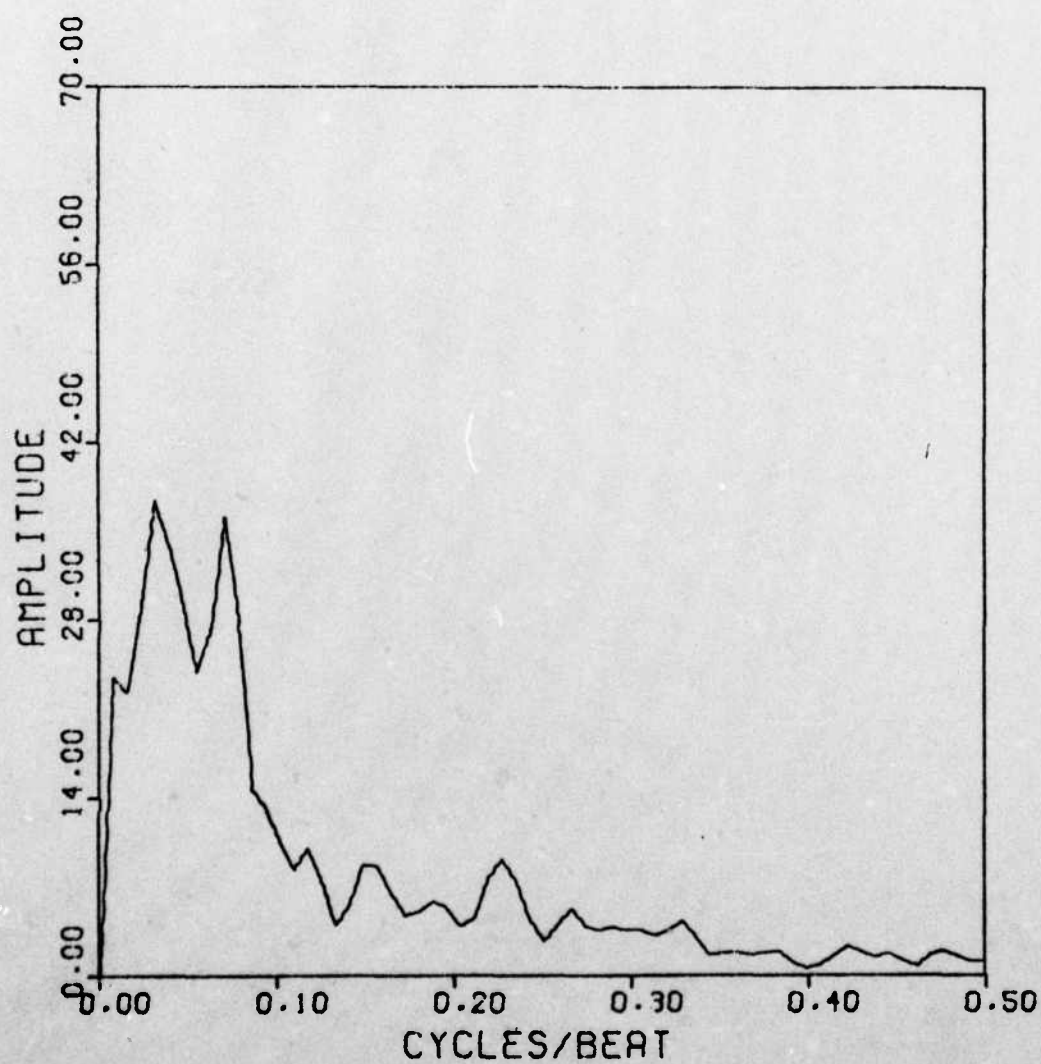
Transition Epoch
Figure 29

LES-OWN-FER
NIGHTS 1,2
STAGES 4-0



Transition Epoch
Figure 30

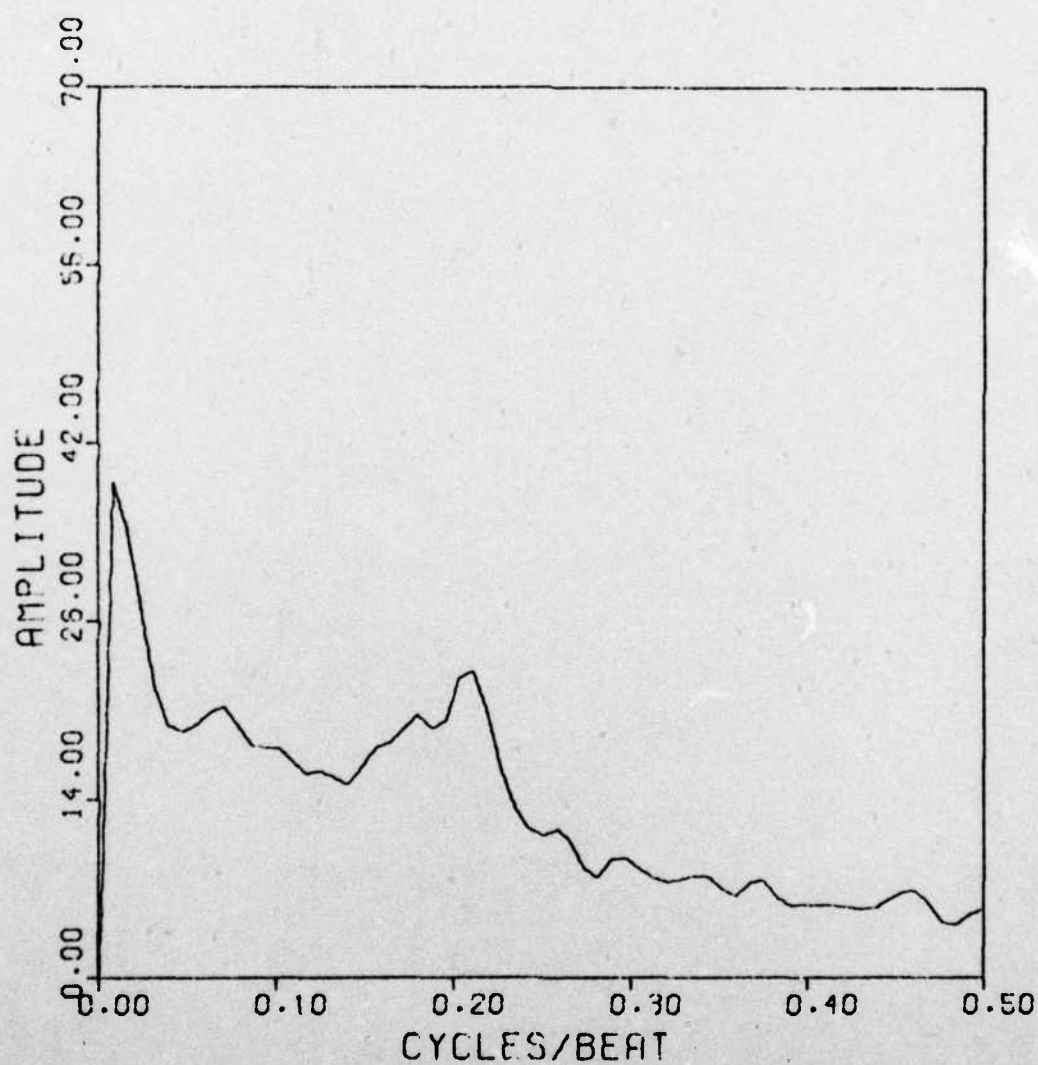
LES-OWN-FER
NIGHTS 1.2
STAGES 4-1



Transition Epoch

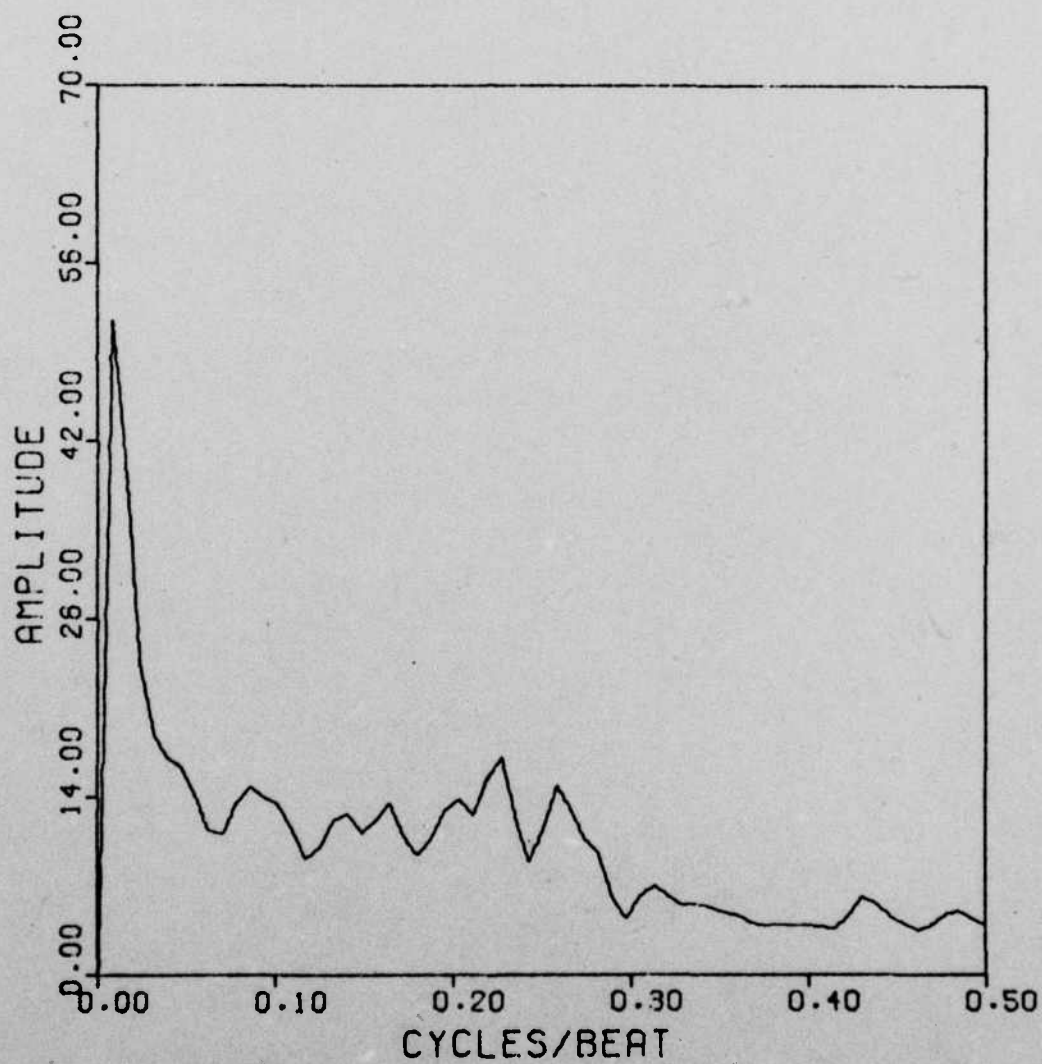
Figure 31

LES-OWN-FER
NIGHTS 1.2
STAGES 4-2

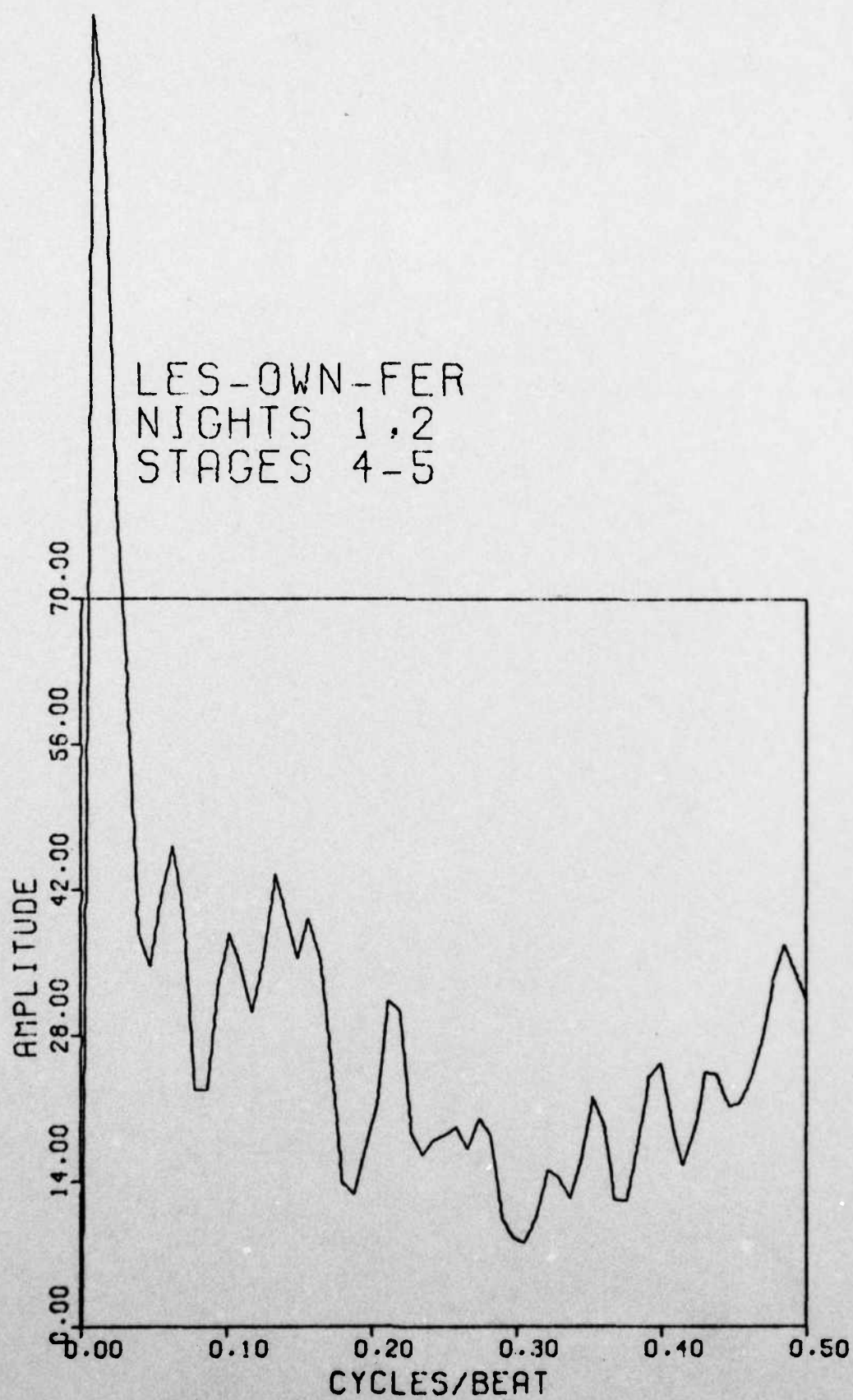


Transition Epoch
Figure 32

LES-OWN-FER
NIGHTS 1,2
STAGES 4-3



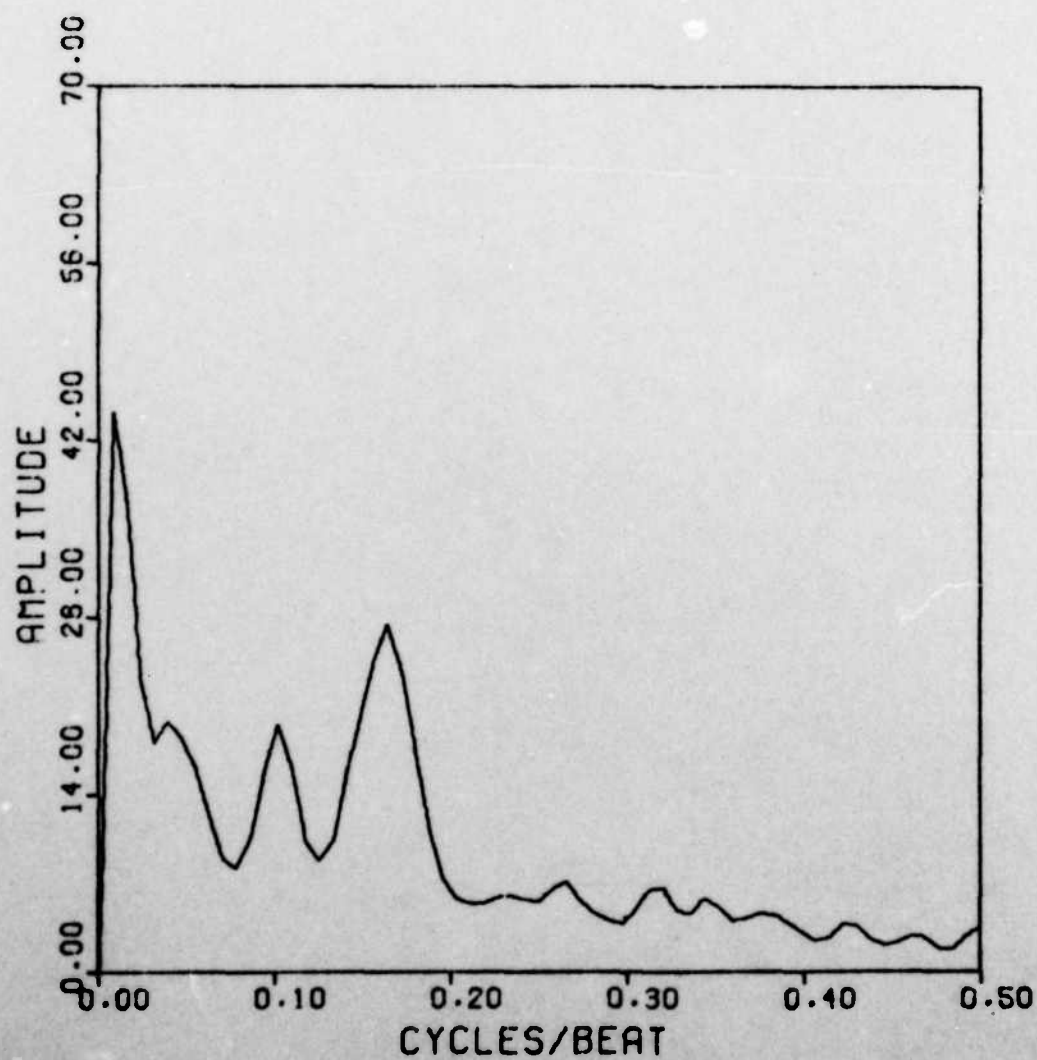
Transition Epoch
Figure 33



Transition Epoch

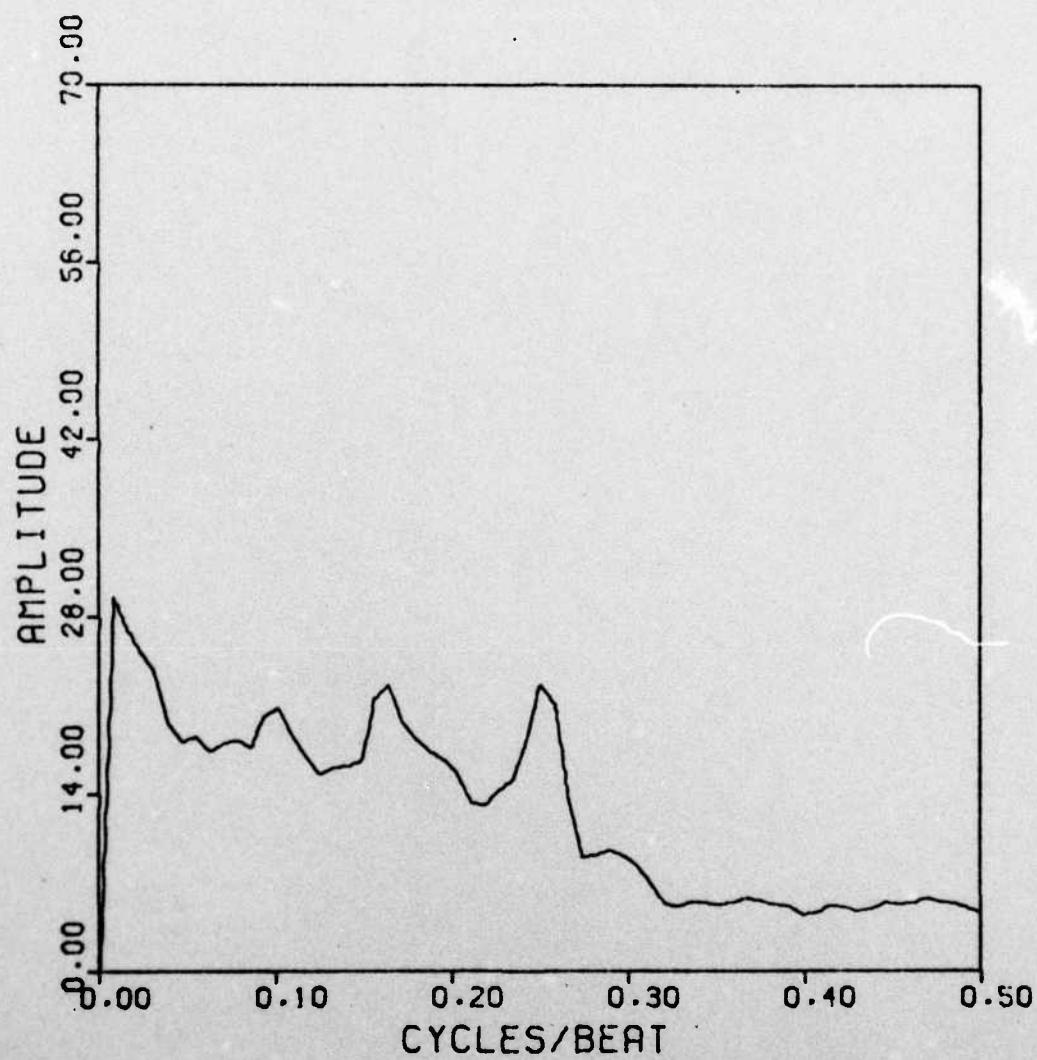
Figure 34

LES-OWN-FER
NIGHTS 1,2
STAGES 5-0



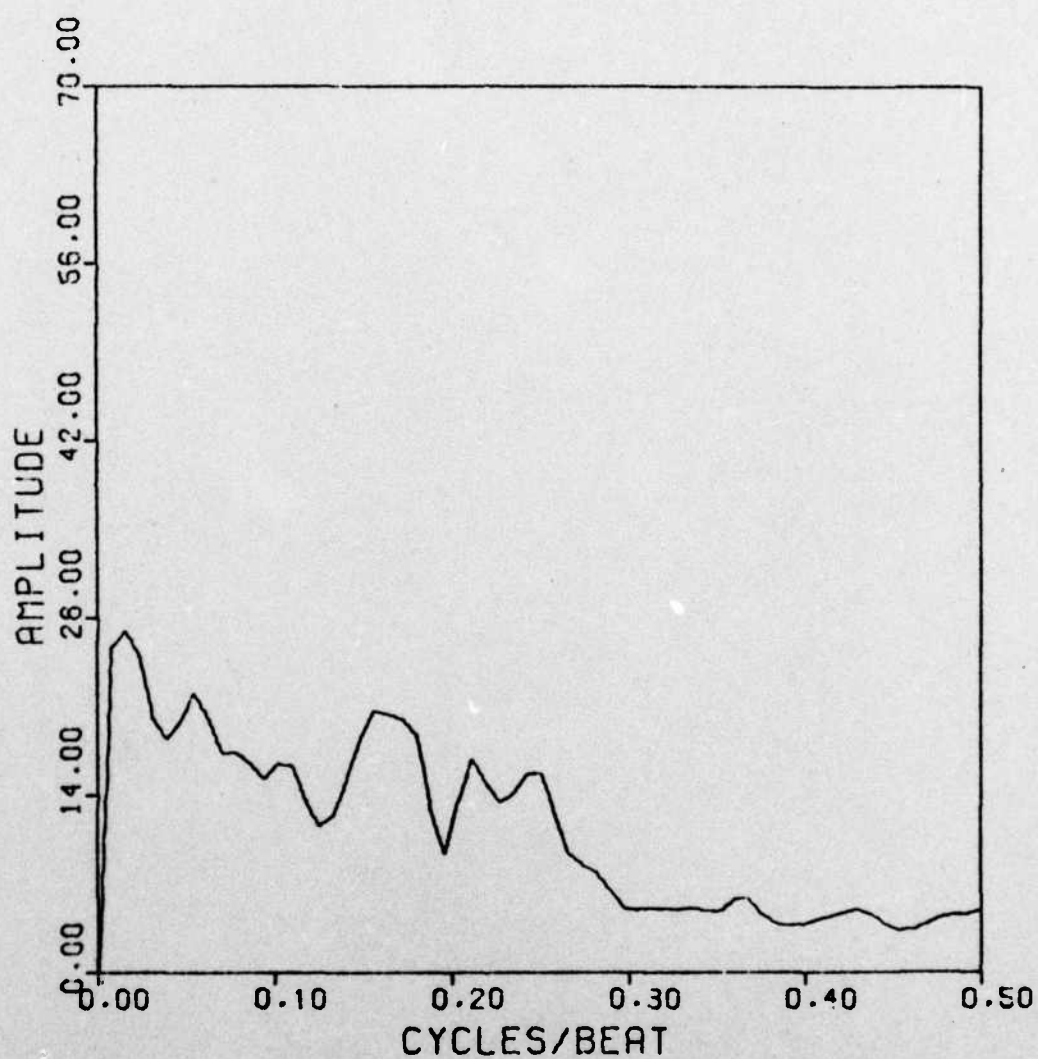
Transition Epoch
Figure 35

LES-OWN-FER
NIGHTS 1,2
STAGES 5-1



Transition Epoch
Figure 36

LES-OWN-FER
NIGHTS 1,2
STAGES 5-2



Transition Epoch
Figure 37

The REM and NREM templates derived from Night 1 of Subject LES and FER to classify subsequent nights of the same subjects. This, in essence, tests the model's ability to classify new data for a given set of subjects upon whom the model was trained.

Phase III - Part 2

This portion of the study tested the REM-NREM classification model on one subject's data which was not used in any way during the training of the model. Five nights of data from Subject OWN were used during these tests.

Phase III - Part 3

This part of our testing phase involved the blind classification (unknown sleep stages) of data from subject PK supplied by the U.S. Army. The object of this test was to indicate the algorithm's effectiveness on long segments of awake data combined with normal sleep data.

CHAPTER V

RESULTS

The results of Phase III - Part 1 for Subjects LES and FER are shown in Tables 11 and 12 respectively. Seven nights of data for Subject LES are shown in Table 11. From a total of 1,062 128-beat intervals of data for Subject LES, a total of 658 128-beat intervals were correctly classified. One hundred sixty-six 128-beat intervals were misclassified as Stage NREM when it was actually Stage REM⁺, while 165 REM⁺ intervals were misclassified. A total of 73 128-beat intervals were a combination of both Stage REM⁺ and Stage NREM. As such, these intervals could not be classified using a two stage template classification.

Five nights of data for Subject FER are shown in Table 12. From a total of 977 128-beat intervals, 563 intervals were correctly classified for a per cent correct of 62.49. Ninety-five 128-beat intervals were misclassified as Stage REM⁺ when they were actually Stage NREM, while 243 NREM intervals were misclassified. A total of 76 128-beat intervals were a combination of both Stage REM⁺ and Stage NREM and as such were not classified.

The results of Phase III - Part 2 are shown in Table 13. These results are based upon data which comes from Subject OWN. This subject's data were not used in the formation of stage templates. From a total of 994 128-beat intervals 552 128-beat intervals were correctly classified for a per cent correct of 59.42. A total of 75 REM⁺ 128-beat intervals were misclassified as NREM and 302 NREM 128-beat intervals were misclassified as REM⁺. There were 65 128-beat intervals which were combinations of Stage REM⁺ and Stage NREM and as such were not classified.

Figures 38 through 40 illustrate preliminary prediction results obtained from the first three of eight days of data supplied by the U.S. Army. The independent variable is time in minutes. The dependent variable is a binary state variable labeled REM⁺, corresponding to a combination of Stages 0, 1, and 5 (REM), and NREM, representing a combination of Stages 2, 3, and 4.

SUBJECT LES

Night	REM ⁺ Prediction Correct : Error	NREM Prediction Correct : Error	Number of REM ⁺ - NREM Transitions	Total Correct*	Worst Case % Correct**	Best Case % Correct***
1	16 35	83 35	24	99	51.30	58.58
2	25 33	96 26	7	121	64.71	67.22
3	31 30	104 21	17	135	66.50	72.58
5	21 28	102 26	11	123	65.43	69.49
6	27 25	83 41	7	110	60.11	62.50
7	17 14	53 17	7	70	64.81	69.31
Total	137 165	521 166	73	658	62.55	66.53

* Total does not include transition intervals

** Transition intervals used in calculations

*** Transition intervals not used in calculations

TABLE 11

SUBJECT FER

<u>Night</u>	REM ⁺ Prediction <u>Correct : Error</u>	NREM Prediction <u>Correct : Error</u>	Number of REM ⁺ - NREM Transitions	Total Correct*	Worst Case %Correct**	Best Case %Correct***
1	42 17	79 40	12	121	63.68	67.98
2	22 12	64 67	22	86	45.99	52.12
3	32 24	79 17	14	111	56.63	60.99
4	35 22	91 41	11	126	63.00	66.67
5	44 20	25 48	17	119	58.33	63.64
Total	175 95	388 243	76	563	57.63	62.49

* Total does not include transition intervals

** Transition intervals used in calculations

*** Transition intervals not used in calculations

TABLE 12

SUBJECT OWN

<u>Night.</u>	<u>REM⁺ Prediction</u>		<u>NREM Prediction</u>		<u>REM⁺ - NREM</u>	<u>Total</u>		<u>Worst Case</u>	<u>Best Case</u>
	<u>Correct</u>	<u>: Error</u>	<u>Correct</u>	<u>: Error</u>	<u>Transitions</u>	<u>Correct*</u>	<u>%Correct**</u>	<u>%Correct**</u>	<u>%Correct***</u>
1	24	20	91	71	14	115	52.27	55.83	
2	25	17	102	64	12	127	57.73	61.06	
3	42	17	84	61	11	126	58.60	61.76	
6	41	9	75	74	14	116	54.46	58.29	
7	35	12	33	32	14	68	53.97	60.71	
Total	167	75	385	302	65	552	55.53	59.42	

* Total does not include transition intervals

** Transition intervals used in calculations

*** Transition intervals not used in calculations

TABLE 13

CHAPTER VI

DISCUSSION

REM⁺ - NREM Classification

Considering the fact that beat-by-beat heart rate was our only criteria, we feel that our REM⁺ - NREM classification model performed with considerable success. Of particular note are the accuracies obtained in classification of data from outside the training set. In classifying test data from subjects LES and FER, each of whose first nights were used as training data, accuracies for LES ranged from 58.58% to 72.58% and for FER from 60.99% to 67.98%. The data for subject OWN was completely separate from the training subjects and yet accuracies ranging from 55.83% to 61.76% were accomplished.

The over-classification of REM⁺ contributed to 67.97% of the errors. Table 14 illustrates the distribution of these errors. Again, over-classification of REM⁺ is evidenced by the percentages of Type I errors. The over-classification of NREM (Type II errors) contributed to 32.03% of the errors. There were a total of 1046 128-beat intervals misclassified out of 3033 128-beat intervals, representing 34.49% total error.

There were 214 128-beat intervals which were not classified from the U.S. Navy data. Since the data were originally visually classified by sleep stage on a minute-by-minute basis, there were several 128-beat intervals which crossed the minute-sleep stage transitions. These 214 128-beat intervals represent 7.06% of the available 3033 128-beat intervals. These unclassified intervals were counted as misclassifications with regard to Tables 11, 12, and 13 results for worst case answers. This may be too harsh an assumption to place upon our algorithm.

REM⁺ NREM CLASSIFICATION
ERROR TYPES

<u>Subject</u>	<u>Night</u>	<u>Type 1*</u>	<u>Type 2**</u>
LES	1	35	35
	2	26	33
	3	21	30
	5	26	28
	6	41	25
	7	17	14
FER	1	40	17
	2	67	12
	3	47	24
	4	41	22
	5	48	20
OWN	1	71	20
	2	64	17
	3	61	17
	6	74	9
	7	32	12

* Type 1 Error = Classifying NREM as REM⁺

** Type 2 Error = Classifying REM⁺ as NREM

TABLE 14

Army Data (Unknown Sleep Stages)

The results shown in Figures 38, 39, and 40 are preliminary findings from several days of data from one subject, PK. Upon receipt of the sleep stage classifications from the Army, we will evaluate all data which have been supplied to date in the same manner as the REM⁺ NREM (U.S. Navy) data. Figure 41 illustrates visually scored results for four nights of data from our untrained subject, OWN. The findings shown in Figures 38 through 40 differ from those of Figure 41. We feel that the differences between these data may be due to the very slow heart rate of the subject, PK, shown Figures 38 through 40, compared to subject OWN (Figure 41). The average heart rate for subject PK was over 1250 milliseconds while the average heart rate for subject OWN was 961 milliseconds for stage REM⁺ and 1066 milliseconds for stage NREM. We are investigating further to see if it will be necessary to train on part of subject PK's data before attempting complete classification prediction.

REM+ NREM CLASSIFICATION ARMY DATA SUBJECT PK, FILE 1

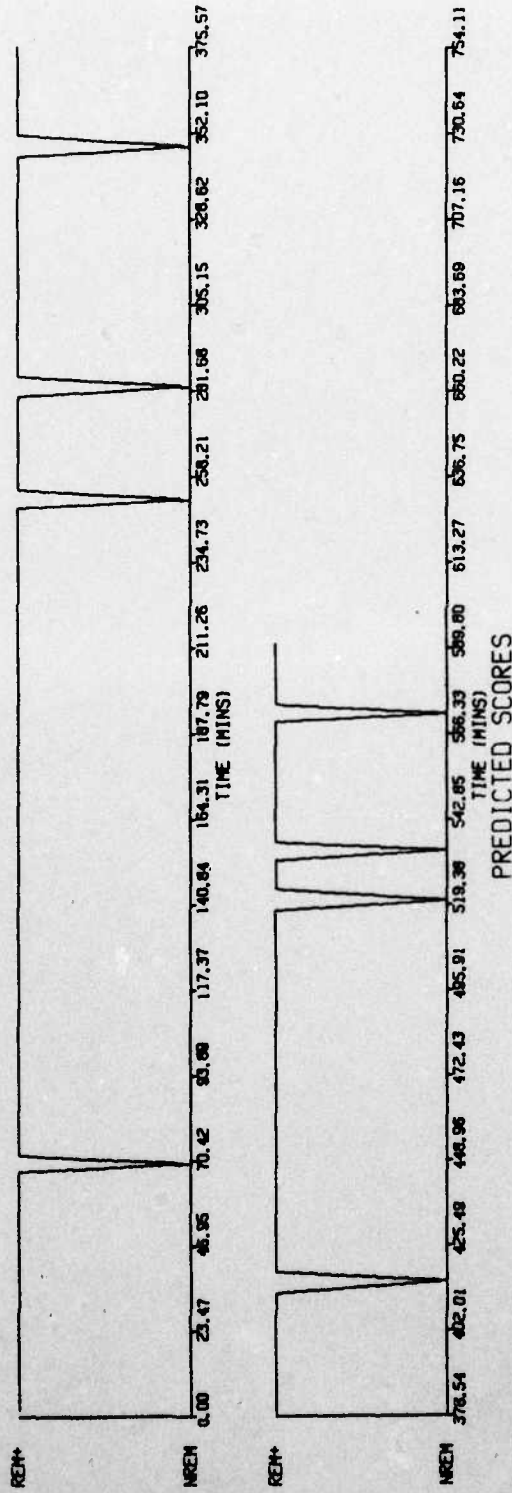


Figure 38

REM+ NREM CLASSIFICATION
ARMY DATA SUBJECT PK, FILE 2

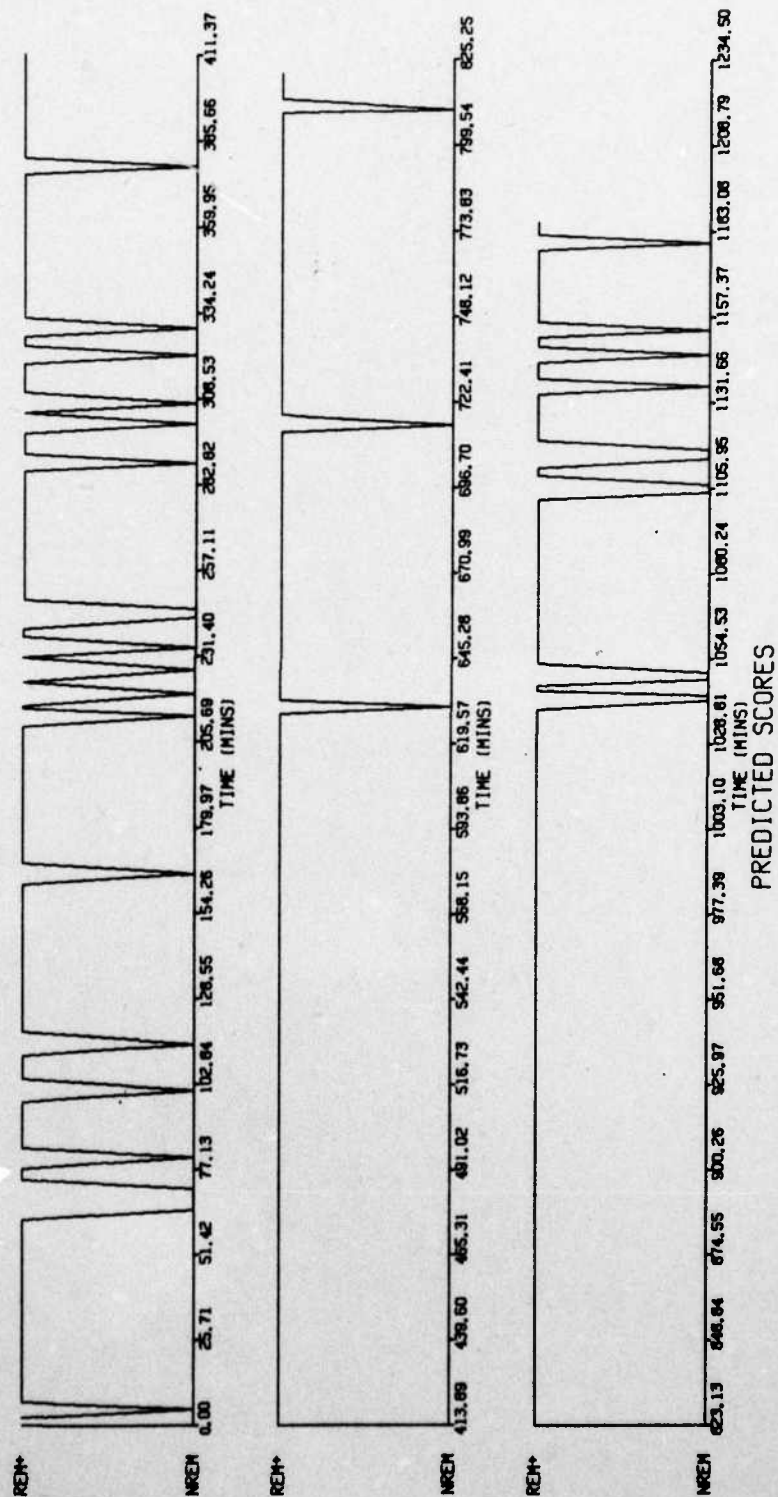


Figure 39

REM+ NREM CLASSIFICATION ARMY DATA SUBJECT PK, FILE 3

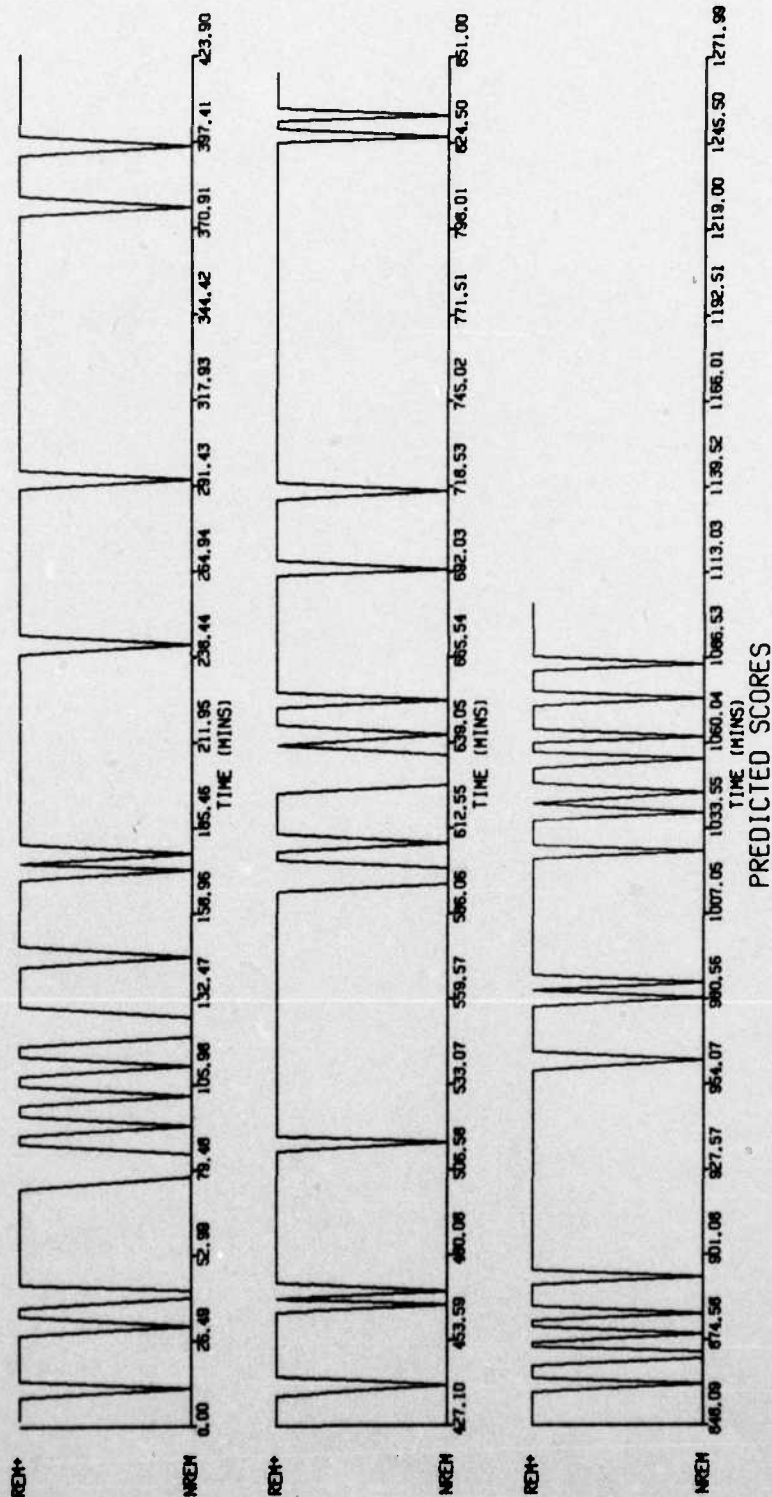
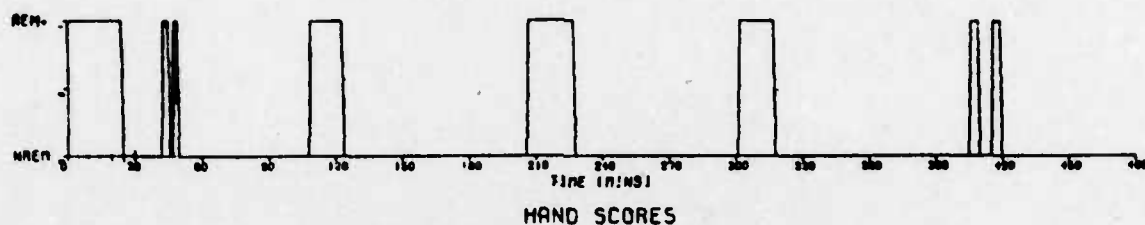
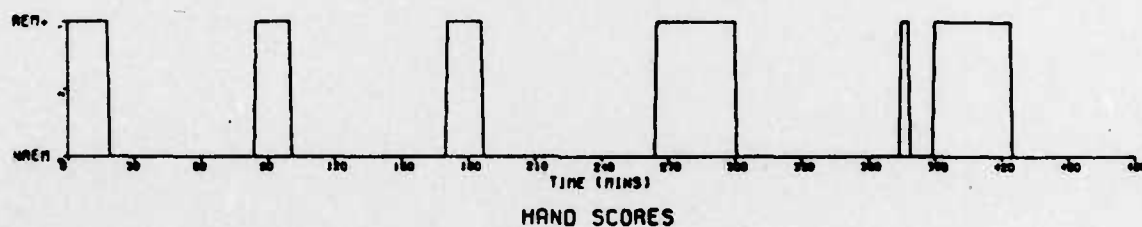


Figure 40

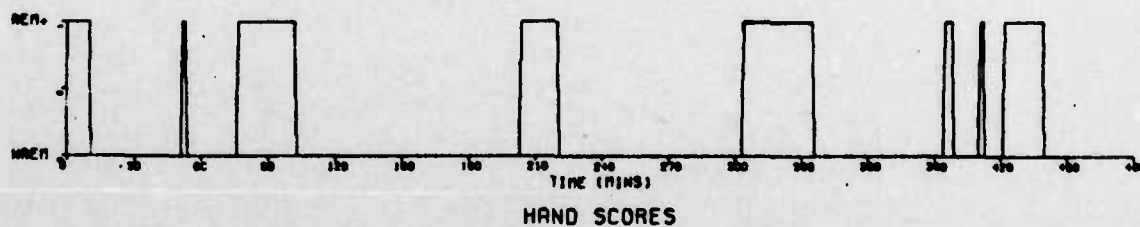
REM-NREM CLASSIFICATION
TRAINING NIGHT 1 SUBJECT OWN



REM-NREM CLASSIFICATION
TRAINING NIGHT 3 SUBJECT OWN



REM-NREM CLASSIFICATION
TRAINING NIGHT 6 SUBJECT OWN



REM-NREM CLASSIFICATION
TRAINING NIGHT 7 SUBJECT OWN

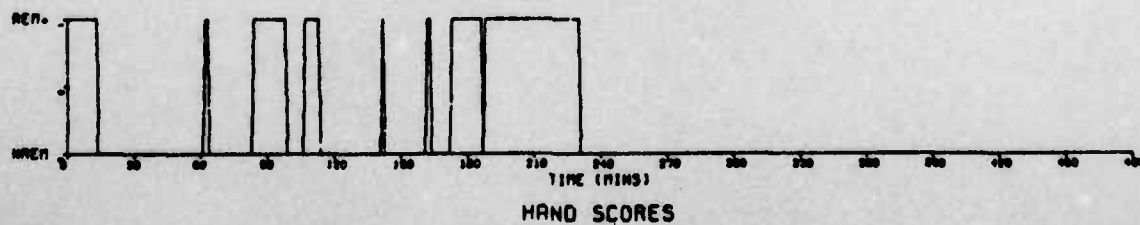


Figure 41

CHAPTER VII

CONCLUSIONS

In summary, we feel that the efforts of this year's research produced the following important results :

- A. We continued development of a new approach to using beat-by-beat heart rate in the classification of sleep patterns. The Beatquency Domain analysis has shown consistent intra- and inter-subject relationships which have proven useful in our investigation.
- B. Considering our results to be successful and encouraging, we have approached one of our primary goals: the reduction of data input and complexity by using an easily derived physiologic parameter.
- C. We feel that while these results are significant, further algorithm development is warranted before the implementation of our algorithm using a microprocessor system.

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SLEEP WAKEFULNESS DETERMINATIONS FROM HEART RATE DATA. VOLUME I--ETC(U)

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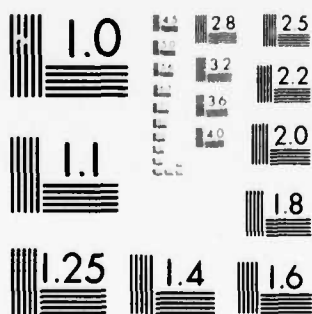
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APPENDIX A

CRITERIA USED FOR DETERMINING
THE R-R INTERVALS IN ANY
GIVEN MINUTE

A. Time Correction

In making the original digital tape containing the R-R intervals in milliseconds for each heartbeat, a total time inconsistency occurred. In other words, the Σ R-R intervals for any given analog tape was not equal to the difference between the start and end times of the digitizing. The Σ R-R intervals was always short by approximately 160 to 200 seconds in every case. Therefore, a time correction factor was introduced to account for this discrepancy.

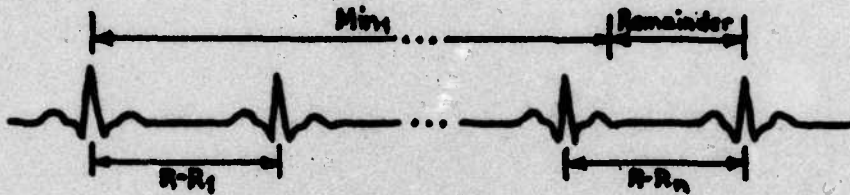
$$T. F. = 1.0 + \frac{\text{Dig. Time} - \text{R-R Time}}{\text{R-R Time}} \quad \text{(Dig. Time \& R-R Time in seconds)}$$

Time correction can be introduced in one of two ways, either multiply each R-R interval by T. F. or multiply 1 minute (60000 msec.) by 1/T.F., thereby making an equivalent minute of slightly less than 60000 msec. Due to reduced error and calculation time, the latter method was used.

B. Determining the R-R's in any Given Minute

It was noted that the start and end times for the R-R digitizing and the hand scoring of sleep stages did not always correspond. Therefore, only those data minutes which had both R-R intervals and associated hand scores were considered.

Consider a typical minute of data as represented below:



Two major assumptions were made in summing R-R intervals:

- (a) Assume that the beginning R wave of R-R₁ falls on the 1st minute marker for minute 1 data.
- (b) Assume that R-R_n belongs to the current minute being processed (in this case, Min₁).

∴ When $\sum_{i=1}^n R_i \geq 60000 \cdot \text{T.F.}$, then n = number of R-R intervals for that minute.

For every succeeding minute after the first, the "Remainder" is included in the summation of R-R's for the next minute, where

$$\text{Remainder} = 60000 \cdot \text{T.F.} - \sum_{i=1}^n R_i$$

Therefore the general equation for Min_j, where $j = 1, 2, 3, \dots$ is when

$$\text{Remainder} + \sum_{i=1}^n R_i \geq 60000 \cdot \text{T.F.}$$

then n = number of R-R intervals for Min_j.

APPENDIX B

SLEEP STAGE CLASSIFICATION FROM PATTERNS IN THE HEART RATE DOMAIN*

The data used for this area of research was the same as were used for the main portion of this report.

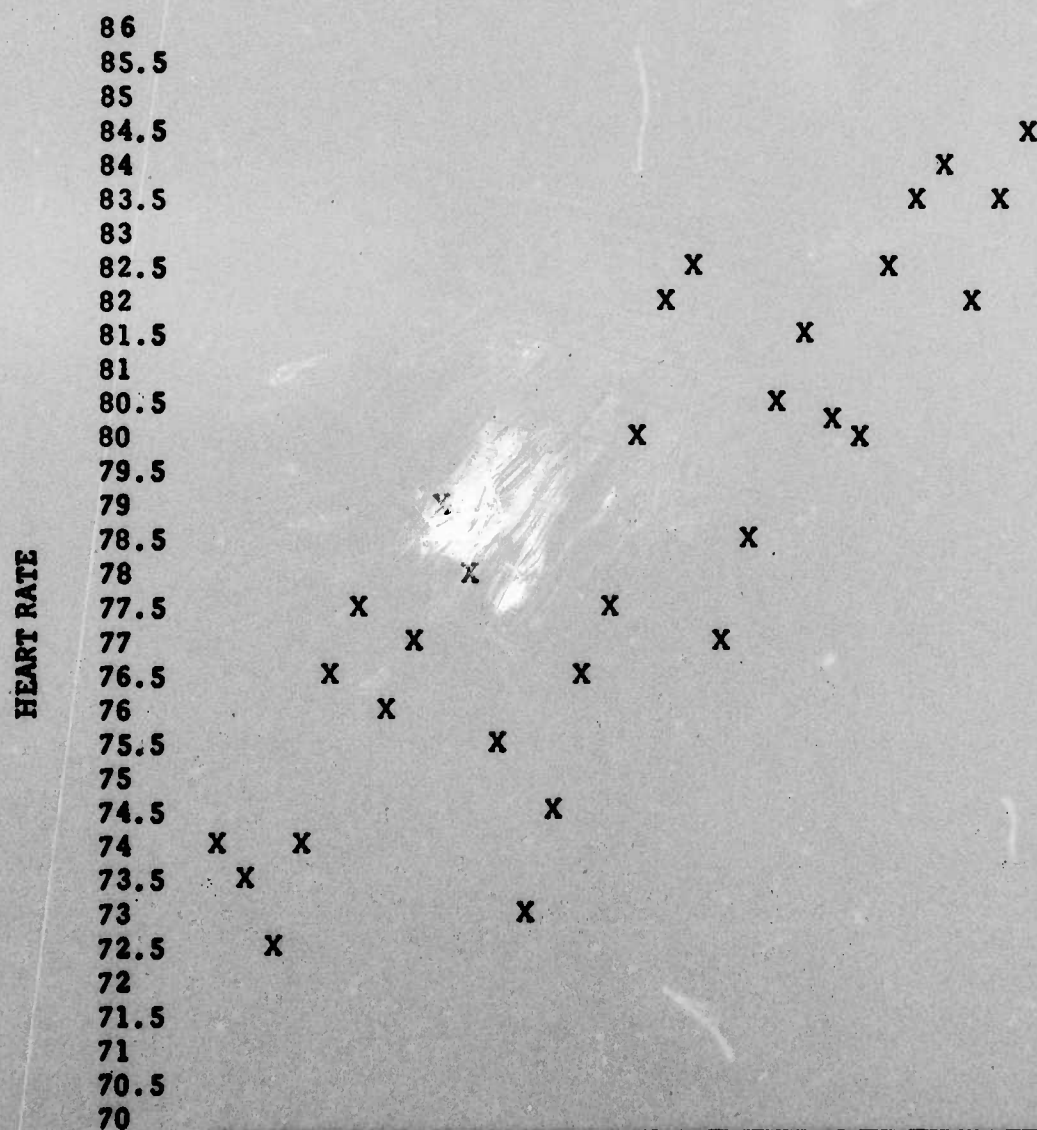
Each night of data for each subject was first analyzed separately using first classification into six separate groups and then classification into three groups. The six groups were awake, stages one through four combined and stage one-REM. The three classification groups were group one, stages awake, one, and one-REM combined; group two, stage two; and group three, combined stages three and four.

For each subject, two nights of data combined were used to form discriminant and classification functions. The classification functions so formed were used to classify each of the remaining nights' records for that subject. The data from these remaining nights were not used in forming the classification equations. Since the actual stage of each minute's sleep was known, the accuracy of the predicted classification of the new data could be evaluated.

PRELIMINARY PROCESSING

Initial analysis of the raw beat by beat heart rate data was made by pattern recognition, identifying as the basic pattern unit a wave described by the heart rate (HR) values between and including successive local minima, as shown in Figure I. Each wave, or cycle, in the form of an inverted V, has a rising edge and falling edge. These edges could be coarsely described in

* Master's Degree Thesis by Randy Joe Montgomery, University of Texas at Austin, December 1976.



SUCCESSIVE INSTANTANEOUS HEART RATES

FIGURE I

terms of a rough measure of their length, the number of intervals between the instantaneous HR values that make up the graph. Any edge of length five or greater was considered to be only of length five. Each cycle then falls into one of twenty-five categories of patterns as described by the lengths of the rising and falling edges. There were five possible types (lengths) of rising edges, and for each of these, five possible types of falling edges. Keeping track of the different types of rising and falling edges separately from each other as individual patterns themselves yielded an additional ten patterns.

The algorithm counted the number of each of these patterns found in each one minute epoch of data, giving thirty-five integer measurements to describe each epoch. Taking each minute as a case assigned to a group according to the EEG scored sleep stage of that minute, and using the 35 measures as discriminating variables, the ability of these variables to differentiate between the EEG scored sleep stages was determined with a linear discriminant analysis routine.

FURTHER FEATURE EXTRACTION

The derivative of the heart rate record, the series of first differences, was produced and subjected to the same pattern recognition and discriminant analysis procedure. Replacing each instantaneous HR value by the difference between it and the previous value formed these differences, as follows:

for $i = 1, n$

$$XD_i = X_i - X_{i-1}$$

where: XD_i = first difference for value
i of the current minute

X_i = HR value for interval i
of the current minute

n = number of HR values in
the minute

$X_{i=0}$ = the last value of the
previous minute

Transforming the data in this way and performing the pattern recognition and counting operations on it also yielded an additional thirty-five measures to be used as discrimination variables for each epoch. Merging the results of these two manipulations provided seventy measures for each minute of sleep.

DISCRIMINANT ANALYSIS PROCEDURE

The linear discriminant analysis program from the SPSS* library evaluated these measures as to their significance and ability to differentiate between the groups as determined sleep stage. The discriminant analysis attempted to make the groups as statistically distinct as possible by weighting and linearly combining the 70 input measures. A number of discriminant functions were formed from the weighting coefficients and standardized values of the discriminating variables, in the following form:

$$D_i = d_{i1}Z_1 + d_{i2}Z_2 + \dots + d_{ip}Z_p$$

where: D_i = score on discriminant function i
 d = weighting coefficient
 Z = standardized values of discriminating variables
 p = number of discriminating variables

Averaging the resulting scores for the minutes within a sleep stage group gave a mean for each discriminant function for each sleep stage. A centroid for each sleep stage was formed from the means of all the discriminant functions for that group. The centroid represented a point in an n -dimensional space where n was the number of discriminant functions used.

The discriminant routine did not use all of the seventy available variables but rejected those which did not contain any useful information. From the various criteria available to evaluate the usefulness of the variables,

* Statistical Package for the Social Sciences - NIE, NH, C.H. Hull, J.G. Jenkins, K. Steinbrenner, D.H. Bent, McGraw-Hill, 1970, ISBN 0-07-046531-2

we chose to use Rao's V , a generalized measure of the overall group separation or distance between centroids. A stepwise selection procedure selected one variable at a time to be included in the analysis. This procedure entered into the analysis the measure which in combination with those variables already chosen best satisfied the statistical criterion for inclusion, in this case, maximization of Rao's V . Using the selected variables, the pooled within groups covariance matrix, and the centroids, a classification equation was formed for each group, of the form:

$$C_i = c_{i1}V_1 + c_{i2}V_2 + \dots + c_{ip}V_p + c_{i0}$$

where: C_i = classification score for group i

c_{ij} = classification coefficients

c_{i0} = a constant

V_k = raw scores of the discriminating
variables

After examining each case and evaluating the classification scores for all possible groups, the case was assigned to the group with the highest classification score, after the scores were adjusted for group size. Cases were more likely to be assigned to larger groups. The group membership of the case as determined by this method can be compared with the actual group membership, which was used to form the equation in the first place.

RESULTS

Table B-1 contains a summary of the classification results for each individual night of data. For each night, the algorithm was used to classify that night's data, showing the degree to which the variables were capable of differentiating between sleep stages. This was done using six individual stages and three groups of stages. Table B-2 summarizes the results of the attempts to use an algorithm trained on two nights of each

SUMMARY OF CLASSIFICATION RESULTS

SINGLE NIGHTS INDIVIDUALLY

	<u>SIX GROUPS*</u>	<u>THREE GROUPS*</u>
SUBJECT LES NIGHT 1	81.5	83.7
SUBJECT LES NIGHT 2	76.1	74.0
SUBJECT LES NIGHT 5	73.7	75.4
SUBJECT LES NIGHT 6	76.8	79.6
SUBJECT LES NIGHT 7	83.0	84.8
SUBJECT FER NIGHT 1	75.4	78.8
SUBJECT FER NIGHT 2	69.7	70.2
SUBJECT FER NIGHT 3	62.6	64.5
SUBJECT FER NIGHT 4	71.9	76.0
SUBJECT FER NIGHT 5	67.4	72.5
SUBJECT OWN NIGHT 1	73.7	76.1
SUBJECT OWN NIGHT 3	72.4	74.3
SUBJECT OWN NIGHT 6	71.9	71.7
SUBJECT OWN NIGHT 7	71.7	75.2

* Values are the percent of epochs in a night classified correctly.

TABLE B - 1

SUMMARY OF CLASSIFICATION RESULTS
ALGORITHM TRAINED ON PREVIOUS NIGHTS

	<u>SIX GROUPS*</u>	<u>THREE GROUPS*</u>
Algorithm trained on subject LES nights 1 and 2:		
SUBJECT LES NIGHT 5	59.2	67.9
SUBJECT LES NIGHT 6	59.3	67.4
SUBJECT LES NIGHT 7	37.7	49.3
Algorithm trained on subject FER nights 1 and 2:		
SUBJECT FER NIGHT 3	47.8	52.6
SUBJECT FER NIGHT 4	57.1	64.0
SUBJECT FER NIGHT 5	54.2	62.9
Algorithm trained on subject OWN nights 1 and 3:		
SUBJECT OWN NIGHT 6	55.1	57.8
SUBJECT OWN NIGHT 7	41.7	59.1

* Values are the percent of epochs in a night classified correctly.

TABLE B - 2

subject's data to classify the remaining data from that subject into sleep stages. This was also done using both six stages and three groups of stages.

DISCUSSION

Visual examination of an instantaneous heart rate graph was made in hopes of noting some consistent characteristic common to each stage, or at least to suggest some parameters worthy of further study to determine their value at discrimination between stages. The graph possessed a definite cyclic characteristic, that is, three or four heart rate (HR) values would each be greater than the one before them, then the following two or three would be slower. The most apparent changes between stages were variations in the regularity and periodicity of the cycles. The lengths of the rising or falling edges seldom exceeded four intervals, so no great amount of information was lost by grouping together all edges of length five or greater to be described as length five.

The linear discriminant program performed separate analysis on the thirty-five measures from the original HR record and the thirty-five measures from the derivative of the original HR record. The original HR record yielded mediocre success at classification, and the measures from the derivative record alone were generally about five per cent more successful, suggesting perhaps that it was a more fundamental quantity. Selecting the best variables from the combined pool of both sets of measures produced further gains in accuracy, so both were used in the final analysis, whose results are shown in Figures B-1 and B-2.

CONCLUSION

A number of psychophysiological measures vary greatly during a night of sleep in humans. Though these measures are somewhat independent, they tend to occur in particular relationship to each other, giving rise to the identification and definition of stages of sleep. With the stages defined

by characteristics of the EEG and EOG as they were in this study, the heart rate signal was found to contain information which at times seemed directly related to sleep stage, and at other times seemed largely independent. The degree of positive relationship between sleep stage and heart rate pattern information was subject to much variation between subjects and in the same subject from night to night. Since the classification of sleep into stages from heart rate data was successful at a level greater than would be expected by chance, we may conclude that the higher level centers responsible for what we observe as stages do have some influence on heart rate phenomena. However, we do not have a basis for the assumption that the heart rate is at all times influenced in a predictable manner by the EEG and EOG defined sleep stages. The evidence seems to be to the contrary, with some suggesting that the consistency of relationship between any individual measure and sleep stages may be mediated by variables as abstract as personality and cognitive style. Further research will be necessary to determine whether more relevant information can be extracted from the heart rate signal or if the difficulties currently encountered are an inherent part of the project.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) During the past years several projects have been conducted at the University of Texas at Austin by members of the Bio-Medical Engineering Program investigating the automated classification of levels of wakefulness. The primary design and goal of these projects was rapid, inexpensive determination of levels of wakefulness performed accurately using easily derived physiologic parameters. It was felt that by combining some of the procedures and results of previous		

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studies with the procedures developed from the last two years of this research, a conglomerate algorithm which had the capabilities desired could be developed.

During the third year of this research, an altered algorithm has been developed from previous algorithms to classify REM - NREM sleep stages from minute-by-minute heart rate. One night of data was used from each of two subjects as training data for our algorithm. The other nights of these two subjects and all the data from a third subject were used as test data. Subjects LES and FER were used as training and test subjects, while subject OWN supplied only test data.

The reclassification of the two training nights yielded accuracies of 51.30% and 63.68% for night one of LES and night one of FER, respectively. Accuracies from the remaining data of subject LES yielded 60.11% to 66.50%, of subject FER 45.99% to 63.68%. Subject OWN, whose data were not used in any training, yielded accuracies from 52.27% to 58.60%.

We concluded from our study that the method of analysis we developed and the results we obtained were sufficient to warrant further investigation. We did achieve one of our primary goals; the reduction of cost, volume, and complexity in automated classification of levels of wakefulness. We feel that further development of an automated process algorithm for the accurate determination of levels of wakefulness can be fulfilled in the foreseeable future.

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